HIV Molecular Immunology 2005

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Preface

Scope and purpose of the HIV molecular immunology database

HIV Molecular Immunology 2005 is an annual companion volume to *HIV Sequence Compendium*. This publication, the 2005 edition, is the printed version of the web-based HIV Immunology Database (`http://www.hiv.lanl.gov/content/immunology/`). The web interface for this relational database has many search options, as well as interactive tools to help immunologists design reagents and interpret their results. We summarize through the previous year's literature, so *HIV Molecular Immunology 2005* has entries through the end of 2004. (There is no *HIV Molecular Immunology 2004*, because we skipped it to make the year in the title match the year of publication.)

In the HIV Immunology Database, HIV-specific B-cell and T-cell responses are summarized and annotated. Immunological responses are divided into three parts, CTL, T helper, and antibody. Within these parts, defined epitopes are organized by protein and binding sites within each protein, moving from left to right through the coding regions spanning the HIV genome. We include human responses to natural HIV infections, as well as vaccine studies in a range of animal models and human trials. Responses that are not specifically defined, such as responses to whole proteins or monoclonal antibody responses to discontinuous epitopes, are summarized at the end of each protein section. Studies describing general HIV responses to the virus, but not to any specific protein, are included at the end of each part.

The annotation includes information such as cross-reactivity, escape mutations, antibody sequence, TCR usage, functional domains that overlap with an epitope, immune response associations with rates of progression and therapy, and how specific epitopes were experimentally defined. Basic information such as HLA specificities for T-cell epitopes, isotypes of monoclonal antibodies, and epitope sequences are included whenever possible. All studies that we can find that incorporate the use of a specific monoclonal antibody are included in the entry for that antibody. A single T-cell epitope can have multiple entries, generally one entry per study.

Finally, maps of all defined linear epitopes relative to the HXB2 reference proteins are provided. Alignments of CTL, helper T-cell, and antibody epitopes are available through the search interface on our web site at `http://www.hiv.lanl.gov/content/immunology`.

Only responses to HIV-1 and HIV-2 are included in the database. CTL responses to SIVs have been periodically summarized in our review section by Dr. Dave Watkins and colleagues. (For their most recent review, please see: Where Have All The Monkeys Gone? Evaluating SIV-Specific CTL in the Post-Mamu-A*01 Era, David H. O'Connor, Todd M. Allen, and David I. Watkins, in the 2001 HIV Immunology compendium). Dr. Christian Brander and colleagues annually provide a concise listing of optimal CTL epitopes. Additional reviews that our editorial board deems of general interest to the HIV research immunology community are solicited each year. This year's reviews are printed in the first part of this database; reviews from previous years can be found at `http://www.hiv.lanl.gov/content/hiv-db/REVIEWS/reviews.html`.

Comments on the database or requests for the hard copy can be sent via email to `immuno@lanl.gov`.

Citing the database

This publication may be cited as

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About the cover

This is a photograph of a young sooty mangabey named Siva taken in the Taï forest. The Taï National Park is situated in the southwest of the Ivory Coast. Sooty mangabeys harbor an SIV related to the human HIV-2 epidemic (see Santiago *et al.*[1]). The photograph was generously donated to the immunology data-

[1] M. L. Santiago, F. Range, B. F. Keele, Y. Li, E. Bailes, F. Bibollet-Ruche, C. Fruteau, R. Noë, M. Peeters, J. F. Brookfield, G. M. Shaw, P. M. Sharp, & B. H. Hahn, 2005. Simian immunodeficiency virus infection in free-ranging sooty mangabeys (*Cercocebus atys atys*) from the Taï Forest, Côte d'Ivoire: Implications for the origin of epidemic human immunodeficiency virus type 2. *J Virol* **79**(19):12515-12527

base by the photographer, Florian Möllers[2], and was taken in the context of the Taï Monkey Project, which is associated with the Centre Suisse de Recherches Scientifiques (CSRS) in Abidjan[3].

Our thanks to Ronald Noë, Florian Möllers, and Beatrice Hahn for making this cover possible.

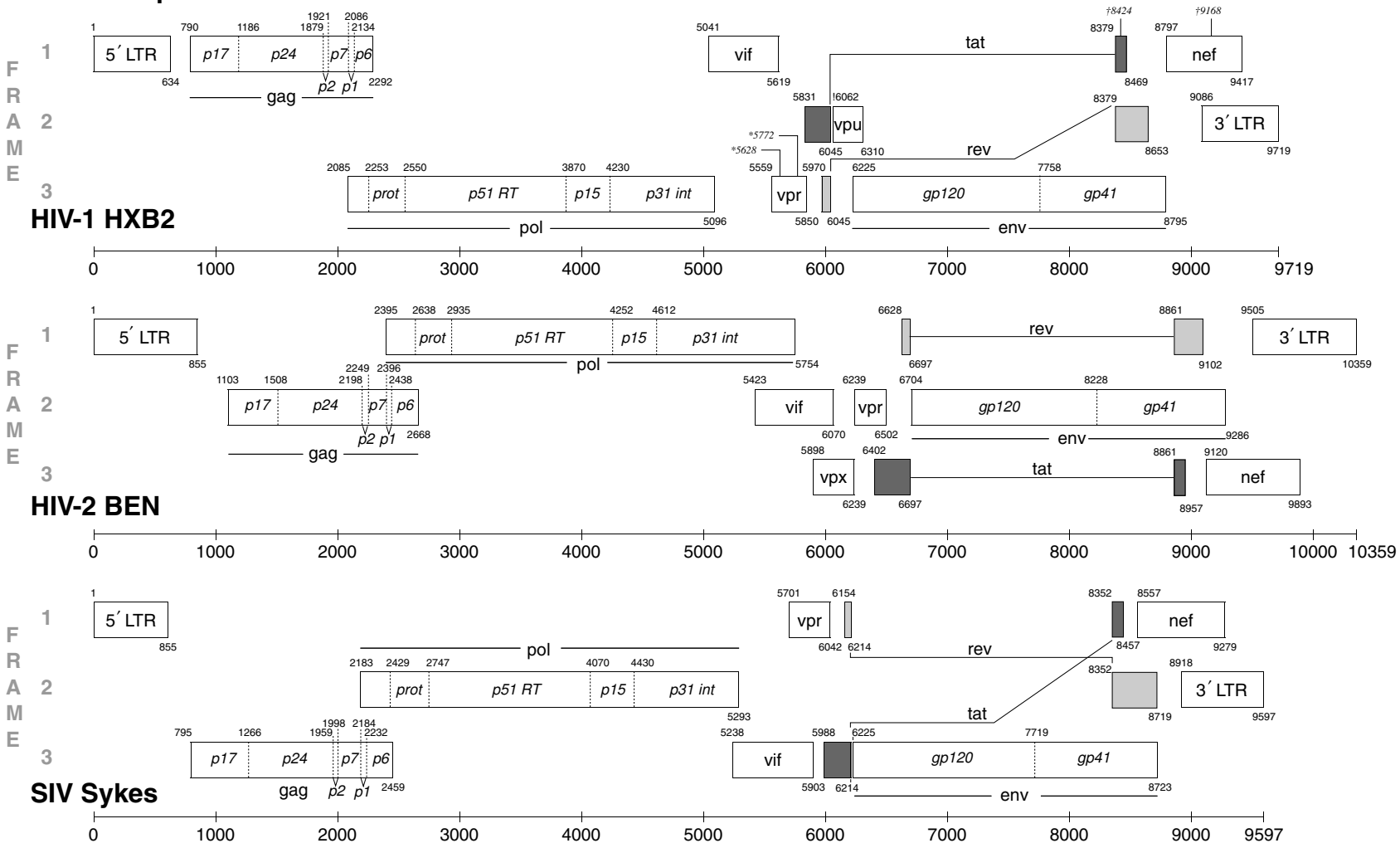
About the PDF

The complete *HIV Molecular Immunology 2005* is available in Adobe Portable Document Format (PDF) from our website, `http://www.hiv.lanl.gov/content/immunology`. The PDF version is hypertext enabled and features 'clickable' table-of-contents, indexes, references and links to external web sites.

This volume is typeset using LaTeX. The immunology data tables and epitope maps are produced automatically from the SQL database by a series of Perl programs.

[2] `http://www.florianmoellers.com/`
[3] `http://www.orn.mpg.de/~knauer/noe/noe.html`

Genome maps



Landmarks of the HIV-1, HIV-2, and SIV genomes. The gene start, indicated by the small number in the upper left corner of each rectangle, normally records the position of the a in the atg start codon for that gene while the number in the lower right records the last position of the stop codon. For *pol*, the start is taken to be the first t in the sequence tttttag which forms part of the stem loop that potentiates ribosomal slippage on the RNA and a resulting −1 frameshift and the translation of the Gag-Pol polyprotein. The *tat* and *rev* spliced exons are shown as shaded rectangles. In HXB2, *5628 and *5772 mark positions of frameshifts in the *vpr* gene; !6062 indicates a defective acg start codon in *vpu*; †8424 and †9168 mark premature stop codons in *tat* and *nef*. See Korber *et al.*, Numbering Positions in HIV Relative to HXB2CG, in *Human Retroviruses and AIDS*, 1998, p. 102. Available from http://www.hiv.lanl.gov/content/hiv-db/REVIEWS/HXB2.html

HIV/SIV proteins

Name	Size	Function	Localization
Gag MA	p17	membrane anchoring; env interaction; nuclear transport of viral core (myristylated protein)	virion
CA	p24	core capsid	virion
NC	p7	nucleocapsid, binds RNA	virion
	p6	binds Vpr	virion
Protease (PR)	p15	gag/pol cleavage and maturation	virion
Reverse Transcriptase (RT)	p66, p51	reverse transcription	virion
RNase H	(heterodimer)	RNAse H activity	virion
Integrase (IN)		DNA provirus integration	virion
Env	gp120/gp41	external viral glycoproteins bind to CD4 and chemokine co-receptors	plasma membrane, virion envelope
Tat	p16/p14	viral transcriptional transactivator	primarily in nucleolus/nucleus
Rev	p19	RNA transport, stability and utilization factor (phosphoprotein)	primarily in nuleolus/nucleus shuttling between nucleolus and cytoplasm
Vif	p23	viral infectivity factor, inhibits minus-strand viral DNA hypermutation	cytoplasm (cytosol, membranes), virion
Vpr	p10-15	promotes nuclear localization of preintegration complex, inhibits cell division, arrests infected cells at G2/M	virion nucleus (nuclear membrane?)
Vpu	p16	promotes extracellular release of viral particles; degrades CD4 in the ER; (phosphoprotein only in HIV-1 and SIVcpz)	integral membrane protein
Nef	p27-p25	CD4 and class I downregulation (myristylated protein)	plasma membrane, cytoplasm, (virion?)
Vpx	p12-16	Vpr homolog present in HIV-2 and some SIVs, absent in HIV-1	virion (nucleus?)
Tev	p28	tripartite tat-env-rev protein (also named Tnv)	primarily in nucleolus/nucleus

Abbreviations

Common abbreviations and acronyms used in this database.

Abbrev.	Meaning
AA	amino acid
AAV	adeno-associated virus
Ab	antibody
ACTG	AIDS clinical trial group
ADC	AIDS dementia complex
ADCC	antibody-dependent cell-medicated cytotoxicity
ADE	antibody-dependent enhancement
ADRA	Antiviral Drug Resistance Analysis: a program that analyzes your sequences for mutations known to confer drug resistance and links to the records in the database
AIDS	acquired immunodeficiency syndrome
ANN	artificial neural networks
anti MHC	anti major histocompatibility complex
APC	antigen presenting cell
ARC	AIDS related complex
ART	anti-retroviral therapy
AZT	azidothymidine
BIMAS	BioInformatics and Molecular Analysis Section
BIV	bovine immunodeficiency virus
BLAST	Basic Local Alignment Search Tool
CAEV	caprine arthritis/encephalitis virus
CD4BS	CD4 binding site
CD4i	antibody that has enhanced binding to gp120 in the presence of SCD4 (CD4 induced)
CDC	Centers for Disease Control and Prevention
CDR	complementary determining regions
CFA	complete Freund's adjuvant
CHI	Center for HIV Information
CMI	cell-mediated immunity
CMV	cytomegaliovirus
CNS	central nervous system
CP	canary pox
CRF	circulating recombinant form
CsA	cyclosporine A
CSF	cerebrospinal fluid
CTL	cytotoxic T lymphocyte
CTLe	CTL effector
CTLp	CTL precursor
CyPA	cyclophilin A
DC	dendritic cell
DDDP	DNA-dependent DNA polymerase
DHH	U. S. Department of Health and Human Services
dMM	deopymannojirimycin
dpc	days post challenge
DTT	dithiothrietol
EIA	enzyme immuno assay
EIAV	equine infectious anemia virus
ELF	Epitope Location Finder
ELISA	Enzyme Linked ImmunoSorbent Assay
ER	endoplasmic reticulum
Fabs	fragment antigen binding-univalent antibody fragment
FASTA format	Fast Alignment Search Tools Anything
FIV	feline immunodeficiency virus
FP	fowl pox
FSW	female sex worker
GALT	gut-associated lymphoid tissues
GDE format	Genetic Data Environment
gp	glycoprotein
GRIV	genetic resistance to HIV
HAART	highly-active anti-retroviral therapy
HCV	hepatitis C virus
HEPS	HIV-exposed persistently seronegative
HIV	human immunodeficiency virus
HIVD	HIV-1 dementia
HLA	human leukocyte antigens
HLA-MHC	human leukocyte antigens-major histocompatibility complex
HMM	hidden Markov models
IAVI	International AIDS Vaccine Initiative
IE genes	immediate early genes
IFA	incomplete Freund's adjuvant
IFN	interferon
IG format	IntelliGenetics format
Ig	immunoglobulin
IL	interleukin
INHI	immunologically normal HIV-infected
iscom	immunostimulating complex
KLH	keyhole limpet hemocyanin
LANL	Los Alamos National Laboratory
LDA	limiting dilution assay
LN	lymph node
LPR	lymphoproliferative response
LT	labile enterotoxin
LTMP	long-term non-progressor
LTR	long terminal repeat
LTS	long term survivor
mAb	monoclonal antibody
MBL	mannose-binding lectin
MCMC	Markov chain Monte Carlo
MDP	muramyl dipeptide
MEI	multiple epitope immunogen
MHC	major histocompatibility complex
MHR	major homology region
ML	maximum likelihood
MLV	murine leukemia virus
MP	maximum parsimony
mpc	months post challenge

Abbrev.	Meaning
MRC	Medical Research Council, UK
MSF	multiple sequence alignment format of the GCG sequence analysis package
MV	measles vector
MVA vector	modified vaccinia virus Ankara
Nab	neutralizing antibody
NCBI	National Center for Biotechnology Information
NIAID	National Institute of Allergies and Infectious Diseases
NIBSC	National Institute for Biological Standards and Control, UK
NIH	National Institutes of Health
NIST	National Institute of Standards and Technology
NJ	neighbor joining
NLS	nuclear localization signal
NRP	non-rapid progressor
NSI	non-synctium-inducing
p	protein
PB	peripheral blood
PBL	peripheral blood lymphocyte
PBMC	peripheral blood mononuclear cell
PCOORD	principal coordinate analysis
PCR	polymerase chain reaction
PERV	porcine endogenous retrovirus
PHYLIP	Phylogeny Inference Package
PL	proteoliposome
RAC	ricin A chain
RDDP	RNA-dependent DNA polymerase
rec/r	recombinant
RIP	Recombinant Identification Program: a program for detecting evidence of inter-subtype recombination
RIPA	Radio Immuno Precipitation Assay
RP	rapid progressor
RRE	Rev-responsive element
rsgp160	recombinant soluble gp160
RSV	Rous sarcoma virus
SAM	Sequence Alignment and Modeling program
SAP	sequential antigen panning
sCD4	soluble CD4
scFv	single-chain variable fragment
SDS	sodium duodecyl sulfate
SFV	Semliki Forest virus
SI	synctium inducing
SIV	simian immunodeficiency virus
SIVE	SIV encephalitis
SNAP	synonymous-nonsynonymous analysis program
STI	supervised treatment interruption (also seen as structured treatment interruption and standard treatment interruption)
TCLA	T cell line adapted
TCR	T-cell receptor
Th	T-helper cell
TNF	tumor necrosis factor
VEE	Venezuelan equine encephalitis
VESPA	Viral Epidemiology Signature Pattern Analysis
VIP	vasoactive intestinal peptide
VL	viral load
VLP	virus like particle, assembled from p55 gag
VSV	vesicular stomatitis virus
VV	vaccinia virus
WB	Western Blot

Amino Acid Codes

A	Alanine
B	Aspartic Acid or Asparagine
C	Cysteine
D	Aspartic Acid
E	Glutamic Acid
F	Phenylalanine
G	Glycine
H	Histidine
I	Isoleucine
K	Lysine
L	Leucine
M	Methionine
N	Asparagine
P	Proline
Q	Glutamine
R	Arginine
S	Serine
T	Threonine
V	Valine
W	Tryptophan
X	unknown or “other” amino acid
Y	Tyrosine
Z	Glutamic Acid or Glutamine
.	gap
-	identity
$	stop codon
#	frameshift

Part I

Review Articles

I-A

Optimal CTL Epitope Identification in HIV Clade B and Non-Clade B Infection

Nicole Frahm[a], **Christian Brander**[a]

I-A-1 T cell immunity in HIV infection

HIV specific cytotoxic T lymphocytes (CTL) and T-helper cells (Th) remain one of the cornerstones of a potential HIV vaccine, and a number of vaccine trials and recent *in vitro* studies point towards the importance of the close interplay between these two arms of the cellular immune response in HIV infection. As more and more vaccine candidates find their way to clinical trials, not only the question of vaccine immunogen selection but also that of the appropriate *in vitro* monitoring of vaccine success become increasingly critical issues. The chosen approaches will need to balance the optimal sensitivity with the need of inter-trial comparability, and several efforts are under way to establish widely applicable *in vitro* antigen test sets to monitor several parallel vaccine trials in the future. The challenge for this undertaking is considerable, given that many vaccine trials are based on non-clade B immunogens, and thus require a comprehensive knowledge of immunogenic regions in various HIV clades, with the most pressing one likely being clade C. Part of this characterization will be the detailed delineation of the optimal CTL epitopes and their HLA restriction that are contained in these regions, so that reliable predictions can be made in terms of population coverage and how well local viral diversity is reflected by the vaccine sequence(s). Thus, although few laboratories nowadays follow through on identifying the precise nature of the targeted, optimal CTL epitopes in their various immunogens, we feel that epitope definition is not only desirable but actually urgently needed for an optimal vaccine design and appropriate analyses of induced responses. As in the past years, we here present an updated compilation of optimally defined CTL epitopes in all regions of HIV, which increasingly also includes epitopes defined in non-clade B infection. As argued above, especially non-clade B derived CTL epitopes will be most useful in refining vaccine approaches in the future and we thus include annotations to the epitopes indicating the test sequence used to identify the epitope. We feel that both of these additional pieces of information are important considerations as they can profoundly impact the detection rate of responses *in vivo* and obviously need to be included in vaccine immunogen design as well.

I-A-2 Escape from CTL recognition and antigen processing

Aside from sequence differences between various HIV clades, much focus has been given over the last few years to sequence variability within defined optimal epitopes as well as to regions in close proximity of such well-defined epitopes. Changes within the epitope are generally interpreted as CTL escape variants that either modulate binding to the HLA molecule or which reduce the binding affinity to the cognate T cell receptor [Brander *et al.*, 1998; Leslie *et al.*, 2004]. On the other hand, changes flanking the epitope, (as well as within) have been shown to interfere with efficient antigen processing, thereby also affording escape from CTL surveillance [Allen *et al.*, 2004; Draenert *et al.*, 2004b]. While CTL escape by changes within the targeted epitope has been well documented and used to link HIV evolution and host genetics [Moore *et al.*, 2002], the importance of processing escape is still unclear. However, processing may represent an effective escape route as no variant-specific CTL responses can be generated after escape has occurred. By inference from large-genome herpesviruses, which often have dedicated multiple genes towards interfering with antigen processing [Brander & Walker, 2000], this strategy seems to be a successful one and it is feasible that the highly variable HIV genome provides ample opportunities for this kind of immune evasion. This is different when escape occurs within the epitope and the epitope is still processed and presented. Except in cases of escape mutation in dominant anchor positions, these changes may mediate escape from TCR recognition but still bind to the restricting allele, thus allowing for the induction of a new population of CTL responses against the escaped variant [Allen *et al.*, 2005; Haas *et al.*, 1996]. Further work will need to be done to assess the frequency and relevance of processing escape, but existing and in

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some cases quite dramatic examples of TCR and/or HLA binding escape should not conceal this potential strategy. In addition, processing escape will or may already have influenced global viral evolution in different ways than CTL escape as other, likely more limited genetic polymorphisms (TAP for instance) may be imprinted on the viral sequences. These considerations can have profound implications for vaccine development and may complicate immunogen sequence design considerably, and the discrimination between processing and CTL escape depends on an accurate description of the actual presented epitopes.

I-A-3 Are "relic" epitopes on the rise?

Adaptation of (viral) pathogens to the human host has been well documented in the past and intensively studied for HIV. Work by a number of laboratories has pointed towards an important role of HLA class I polymorphism and viral evolution, presumably through viral adaptation to HLA class I restricted CTL responses [Altfeld *et al.*, 2005; Leslie *et al.*, 2005; Moore *et al.*, 2002]. A number of studies have in the meantime identified populations with particularly high frequencies of specific HLA class I alleles and associated specific local sequences with escape from CTL epitopes restricted by these common HLA alleles. Such studies include HLA-B57 positive individuals in South Africa, HLA-A24 expression subjects in the Japanese population and others that have been used to track potential CTL epitopes by reverse genetic approaches [Allen *et al.*, 2004; de Oliveira *et al.*, 2004; Furutsuki *et al.*, 2004; Leslie *et al.*, 2005]. Furthermore, in a recent work from our laboratory, population wide adaptation may even have rendered an HLA allele, in this case HLA-B*1503, from being associated with reduced viral load in a population with low allele frequency to a an allele associated with higher than average viral load in the population where it is overly frequent [Frahm *et al.*, 2005b]. However, the kinetics of such population wide adaptation and possible founder effects need to be seriously considered when interpreting these data as similar sequence patterns may emerge in population that do not share specific high frequency alleles [Korber *et al.*, 2005]. Regardless of whether founder effects may, at least partially, be responsible for the observed imprinting, high allele frequencies very likely facilitate the maintenance of escape variants and bear the question as to whether CTL responses restricted by common HLA alleles can be of significant importance for *in vivo* viral control [Lieberman, 2002]. As viral adaptation to any CTL pressure, including that restricted by common alleles, may result in reduced viral fitness and thus reduced *in vivo* viral burden, CTL responses restricted by common alleles may indeed contribute to viral control [Brander & Walker, 2003]. Despite frequent reversion of escaped CTL epitopes in hosts not expressing the restricting allele, especially CTL epitopes restricted by common alleles may be eliminated from the circulating viral population. Inclusion of such "relic" epitopes in vaccine design may for obvious reasons not provide much protection from infection by contemporary, circulating viral isolates and highlights again the need to have well defined epitope maps available for all clades of HIV.

As in the past years, we attempted to adhere for the present listing to a number of criteria that need to be fulfilled for inclusion [Brander & Walker, 1995; Hunziker *et al.*, 1998]. While these criteria should help to ensure proper identification of the minimal epitope targeted at the lowest peptide concentration and provide unequivocal identification of the restricting HLA class I allele, there may still be occasions where the data reported here conflict with data in other laboratories. We would like to encourage any investigator who observes discrepancies in his/her own data with what is reported here to bring this to our attention. Especially, we have reported earlier on cases of epitopes that appear to be presented on more than one allele; a phenomenon that may be more widespread than previously assumed and which may profoundly complicate data interpretation. Such information on additional presenting alleles can be highly useful for other investigators and we would welcome any contribution of this kind. Similarly, as newly identified epitopes may violate known HLA binding motifs or may be embedded in previously described epitope sequences, properly mapped epitopes may help to refine currently incompletely defined allele-specific binding motifs, thereby not only facilitating work in HIV but in other viral infections, cancer and autoimmunity as well.

I-A-4 Table of optimal HIV-1 CTL epitopes

Table I-A.1: Best defined HIV CTL epitopes.

HLA	Protein	AA	Sequence	Reference
A*0101 (A1)	gp160	787–795	RRGWEVLKY	Cao, 2002
A2	RT	127–135	YTAFTIPSV	Draenert, 2004
A*0201 (A2)			2 6 C	Falk *et al.*, 1991; Barouch *et al.*, 1995
		1° anchor	**L** **L**	
			M **V**	
		2° anchor	V	
A*0201 (A2)	p17	77–85	SLYNTVATL	Johnson *et al.*, 1991; Parker *et al.*, 1992, 1994
A*0201 (A2)	p1	1–10	FLGKIWPSYK	Yu *et al.*, 2002b
A*0201 (A2)	RT	33–41	ALVEICTEM	Haas *et al.*, 1998; Haas, 1999
A*0201 (A2)	RT	179–187	VIYQYMDDL	Harrer *et al.*, 1996a
A*0201 (A2)	RT	309–317	ILKEPVHGV	Walker *et al.*, 1989; Tsomides *et al.*, 1991
A*0201 (A2)	Vpr	59–67	AIIRILQQL	Altfeld *et al.*, 2001a,b
A*0201 (A2)	gp160	311–320	RGPGRAFVTI	Alexander-Miller *et al.*, 1996
A*0201 (A2)	gp160	813–822	SLLNATDIAV	Dupuis *et al.*, 1995
A*0201 (A2)	Nef	136–145	PLTFGWCYKL	Haas *et al.*, 1996; Maier & Autran, 1999
A*0201 (A2)	Nef	180–189	VLEWRFDSRL	Haas *et al.*, 1996; Maier & Autran, 1999
A*0202 (A2)			2 C	Barouch *et al.*, 1995
			L **L**	
			V	
A*0202 (A2)	p17	77–85	SLYNTVATL	Goulder, 1999
A*0205 (A2)	p17	77–85	SLYNTVATL	Goulder, 1999
A*0205 (A2)	gp160	846–854	RIRQGLERA	Sabbaj *et al.*, 2003
A*0207 (A2)	p24	164–172	YVDRFYKTL	Currier *et al.*, 2002
A*0301 (A3)	p17	18–26	KIRLRPGGK	Harrer *et al.*, 1996b
A*0301 (A3)	p17	20–28	RLRPGGKKK	Goulder *et al.*, 1997b; Culmann, 1999; Lewinsohn & Riddell, 1999; Wilkes & Ruhl, 1999
A*0301 (A3)	p17	20–29	RLRPGGKKKY	Goulder *et al.*, 2000b
A*0301 (A3)	RT	33–43	ALVEICTEMEK	Haas *et al.*, 1998; Haas, 1999
A*0301 (A3)	RT	73–82	KLVDFRELNK	Yu *et al.*, 2002a
A*0301 (A3)	RT	93–101	GIPHPAGLK	Yu *et al.*, 2002a
A*0301 (A3)	RT	158–166	AIFQSSMTK	Threlkeld *et al.*, 1997
A*0301 (A3)	RT	269–277	QIYPGIKVR	Yu *et al.*, 2002a
A*0301 (A3)	RT	356–366	RMRGAHTNDVK	Yu *et al.*, 2002a
A*0301 (A3)	Integrase	179–188	AVFIHNFKRK	Yu *et al.*, 2002a
A*0301 (A3)	Vif	17–26	RIRTWKSLVK	Altfeld *et al.*, 2001a; Yu *et al.*, 2002a
A*0301 (A3)	Vif	28–36	HMYISKKAK	Yu *et al.*, 2002a
A*0301 (A3)	Vif	158–168	KTKPPLPSVKK	Yu *et al.*, 2002a
A*0301 (A3)	Rev	57–66	ERILSTYLGR	Addo, 2002; Yu *et al.*, 2002a
A*0301 (A3)	gp160	37–46	TVYYGVPVWK	Johnson *et al.*, 1994
A*0301 (A3)	gp160	770–780	RLRDLLLIVTR	Takahashi *et al.*, 1991
A*0301 (A3)	Nef	73–82	QVPLRPMTYK	Koenig *et al.*, 1990; Culmann *et al.*, 1991
A*0301 (A3)	Nef	84–92	AVDLSHFLK	Yu *et al.*, 2002a

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
A*1101 (A11)			2 C **K** V I F Y	Zhang *et al.*, 1993; Rammensee *et al.*, 1995
A*1101 (A11)	p17	84–92	TLYCVHQRI	Harrer *et al.*, 1998
A*1101 (A11)	p24	217–227	ACQGVGGPGHK	Sipsas *et al.*, 1997
A*1101 (A11)	RT	158–166	AIFQSSMTK	Johnson & Walker, 1994; Zhang *et al.*, 1993; Threlkeld *et al.*, 1997
A*1101 (A11)	RT	341–350	IYQEPFKNLK	Culmann, 1999
A*1101 (A11)	RT	520–528	QIIEQLIKK	Fukada *et al.*, 1999
A*1101 (A11)	Integrase	179–188	AVFIHNFKRK	Fukada *et al.*, 1999
A*1101 (A11)	gp160	199–207	SVITQACPK	Fukada *et al.*, 1999
A*1101 (A11)	Nef	73–82	QVPLRPMTYK	Buseyne, 1999
A*1101 (A11)	Nef	75–82	PLRPMTYK	Culmann *et al.*, 1991
A*1101 (A11)	Nef	84–92	AVDLSHFLK	Culmann *et al.*, 1991
A23	gp41	74–82	RYLKDQQLL	Cao *et al.*, 2003
A*2402 (A24)			2 C **Y** **I** **L** **F**	Maier *et al.*, 1994
A*2402 (A24)	p17	28–36	KYKLKHIVW	Ikeda-Moore *et al.*, 1998; Lewinsohn, 1999
A*2402 (A24)	p24	162–172	RDYVDRFFKTL	Dorrell *et al.*, 1999; Rowland-Jones, 1999
A*2402 (A24)	gp160	52–61	LFCASDAKAY	Lieberman *et al.*, 1992; Shankar *et al.*, 1996
A*2402 (A24)	gp160	585–593	RYLKDQQLL	Dai *et al.*, 1992
A*2402 (A24)	Nef	134–141	RYPLTFGW	Goulder *et al.*, 1997a; Ikeda-Moore *et al.*, 1998
A*2501 (A25)	p24	13–23	QAISPRTLNAW	Kurane & West, 1999
A*2501 (A25)	p24	71–80	ETINEEAAEW	Klenerman *et al.*, 1996; van Baalen *et al.*, 1996
A*2601 (A26)			12 6 C **V** **Y** **T** **F** **I** **L** **F** D I E L V	Dumrese *et al.*, 1998
A*2601 (A26)	p24	35–43	EVIPMFSAL	Goulder *et al.*, 1996a
A*2601 (A26)	RT	449–457	ETKLGKAGY	Sabbaj *et al.*, 2003
A29	Nef	120–128	YFPDWQNYT	Draenert *et al.*, 2004a
A*2902 (A29)	p17	78–86	LYNTVATLY	Masemola *et al.*, 2004
A*2902 (A29)	gp160	209–217	SFEPIPIHY	Altfeld, 2000

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
A30	p17	34–44	LVWASRELERF	Masemola *et al.*, 2004
A*3002 (A30)			12 C **Y** **Y** **F** **L** **V** R	Rammensee *et al.*, 1999
A*3002 (A30)	p17	76–86	RSLYNTVATLY	Goulder *et al.*, 2001
A*3002 (A30)	RT	173–181	KQNPDIVIY	Goulder *et al.*, 2001
A*3002 (A30)	RT	263–271	KLNWASQIY	Goulder *et al.*, 2001
A*3002 (A30)	RT	356–365	RMRGAHTNDV	Sabbaj *et al.*, 2003
A*3002 (A30)	Integrase	219–227	KIQNFRVYY	Sabbaj *et al.*, 2003; Rodriguez *et al.*, 2004
A*3002 (A30)	gp160	310–318	HIGPGRAFY	Sabbaj *et al.*, 2003
A*3002 (A30)	gp160	704–712	IVNRNRQGY	Goulder *et al.*, 2001
A*3002 (A30)	gp160	794–802	KYCWNLLQY	Goulder *et al.*, 2001
A*3101 (A31)			2 C **R** L V Y F	Falk *et al.*, 1994; Rammensee *et al.*, 1999
A*3101 (A31)	gp160	770–780	RLRDLLLIVTR	Safrit *et al.*, 1994a,b
A*3201 (A32)	RT	392–401	PIQKETWETW	Harrer *et al.*, 1996b
A*3201 (A32)	gp160	419–427	RIKQIINMW	Harrer *et al.*, 1996b
A33	Nef	133–141	TRYPLTFGW	Cao, 2002
A*3303 (A33)	gp41	187–196	VFAVLSIVNR	Hossain *et al.*, 2001
A*3303 (A33)	gp41	320–327	EVAQRAYR	Hossain *et al.*, 2001
A*3303 (A33)	Vpu	29–37	EYRKILRQR	Addo *et al.*, 2002
A*6801 (A68)	Tat	39–49	ITKGLGISYGR	Oxenius *et al.*, 2002
A*6801 (A68)	Vpr	52–62	DTWAGVEAIIR	Sabbaj *et al.*, 2004
A*6802 (A68)	RT	436–445	GAETFYVDGA	Rathod & Kiepiela, 2005
A*6802 (A68)	Protease	3–11	ITLWQRPLV	Rowland-Jones, 1999
A*6802 (A68)	Protease	30–38	DTVLEEWNL	Rowland-Jones, 1999
A*6802 (A68)	Vpr	48–57	ETYGDTWTGV	Rathod & Kiepiela, 2005
A*6802 (A68)	gp160	777–785	IVTRIVELL	Wilkes, 1999
A*7401 (A19)	Protease	3–11	ITLWQRPLV	Rowland-Jones, 1999

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B7	p24	84–92	HPVHAGPIA	Yu *et al.*, 2002a
B7	RT	156–164	SPAIFQSSM	Frahm & Brander, 2005
B*0702 (B7)			123 C **P** **L** A R **F** R K	Englehard *et al.*, 1993; Rammensee *et al.*, 1999
B*0702 (B7)	p24	16–24	SPRTLNAWV	Lewinsohn, 1999
B*0702 (B7)	p24	48–56	TPQDLNTML	Wilson, 1999; Wilkes *et al.*, 1999; Jin *et al.*, 2000; Wilson *et al.*, 1997
B*0702 (B7)	p24	223–231	GPGHKARVL	Goulder, 1999
B*0702 (B7)	Vpr	34–42	FPRIWLHGL	Altfeld *et al.*, 2001a
B*0702 (B7)	Vif	48–57	HPRVSSEVHI	Altfeld *et al.*, 2001a
B*0702 (B7)	gp160	298–307	RPNNNTRKSI	Safrit *et al.*, 1994b
B*0702 (B7)	gp160	843–851	IPRRIRQGL	Wilkes & Ruhl, 1999
B*0702 (B7)	Nef	68–77	FPVTPQVPLR	Haas *et al.*, 1996; Maier & Autran, 1999
B*0702 (B7)	Nef	68–76	FPVTPQVPL	Bauer *et al.*, 1997; Frahm & Goulder, 2002
B*0702 (B7)	Nef	71–79	TPQVPLRPM	Goulder, 1999
B*0702 (B7)	Nef	77–85	RPMTYKAAL	Bauer *et al.*, 1997
B*0702 (B7)	Nef	106–115	RQDILDLWIY	Goulder, 1999
B*0702 (B7)	Nef	128–137	TPGPGVRYPL	Culmann-Penciolelli *et al.*, 1994; Haas *et al.*, 1996
B8	gp160	848–856	RQGLERALL	Cao, 2002
B*0801 (B8)			23 5 C **K** **K** **L** **R** PR L	Hill *et al.*, 1992; Sutton *et al.*, 1993; DiBrino *et al.*, 1994b
B*0801 (B8)	p17	24–32	GGKKKYKLK	Reid *et al.*, 1996; Goulder *et al.*, 1997d
B*0801 (B8)	p17	74–82	ELRSLYNTV	Goulder *et al.*, 1997d
B*0801 (B8)	p24	128–135	EIYKRWII	Sutton *et al.*, 1993; Goulder *et al.*, 1997d
B*0801 (B8)	p24	197–205	DCKTILKAL	Sutton *et al.*, 1993
B*0801 (B8)	RT	18–26	GPKVKQWPL	Walker *et al.*, 1989; Sutton *et al.*, 1993
B*0801 (B8)	gp160	2–10	RVKEKYQHL	Sipsas *et al.*, 1997
B*0801 (B8)	gp160	586–593	YLKDQQLL	Johnson *et al.*, 1992; Shankar *et al.*, 1996
B*0801 (B8)	Nef	13–20	WPTVRERM	Goulder *et al.*, 1997d
B*0801 (B8)	Nef	90–97	FLKEKGGL	Culmann-Penciolelli *et al.*, 1994; Price *et al.*, 1997
B13	Nef	106–114	RQDILDLWI	Harrer *et al.*, 2005
B14	p2p7p1p6	42–50	CRAPRKKGC	Yu *et al.*, 2002b
B*1402 (B14)			23 5 C **R** **R** **L** **K** **H** L Y F	DiBrino *et al.*, 1994a
B*1402 (B14)	p24	166–174	DRFYKTLRA	Harrer *et al.*, 1996b
B*1402 (B14)	gp160	584–592	ERYLKDQQL	Johnson *et al.*, 1992

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*1501 (B62)			2 C	
			Q Y	Barber *et al.*, 1997
			L F	Barber *et al.*, 1997
			M	Barber *et al.*, 1997
B*1501 (B62)	p24	137–145	GLNKIVRMY	Johnson *et al.*, 1991; Goulder, 1999
B*1501 (B62)	RT	260–271	LVGKLNWASQIY	Johnson, 1999
B*1501 (B62)	RT	309–318	ILKEPVHGVY	Johnson *et al.*, 1991; Johnson, 1999
B*1501 (B62)	Nef	117–127	TQGYFPDWQNY	Culmann, 1999
B*1503 (B72)	p24	24–32	VKVIEEKAF	Honeyborne & Kiepiela, 2005
B*1503 (B72)	p24	164–172	YVDRFFKTL	Masemola *et al.*, 2004
B*1503 (B72)	RT	496–505	VTDSQYALGI	Sabbaj *et al.*, 2003
B*1503 (B72)	Integrase	135–143	IQQEFGIPY	Honeyborne & Kiepiela, 2005
B*1503 (B72)	Integrase	185–194	FKRKGGIGGY	Honeyborne, 2003
B*1503 (B72)	Integrase	263–271	RKAKIIRDY	Cao *et al.*, 2003
B*1503 (B72)	Tat	38–47	FQTKGLGISY	Novitsky *et al.*, 2001
B*1503 (B72)	Nef	183–191	WRFDSRLAF	Cao, 2002
B*1510 (B71)	p24	12–20	HQAISPRTL	Day, 2005
B*1510 (B71)	p24	61–69	GHQAAMQML	Day, 2003
B*1510 (B71)	Vif	79–87	WHLGHVSI	Honeyborne, 2003
B*1516 (B63)			2 9	Barber *et al.*, 1997; Seeger *et al.*, 1998
			T Y	
			S I	
			V	
			F	
B*1516 (B63)	gp160	375–383	SFNCGGEFF	Wilson *et al.*, 1997; Wilson, 1999
B*1801 (B18)	p24	161–170	FRDYVDRFYK	Ogg *et al.*, 1998
B*1801 (B18)	Vif	102–111	LADQLIHLHY	Altfeld *et al.*, 2001a
B*1801 (B18)	Nef	135–143	YPLTFGWCY	Culmann *et al.*, 1991; Culmann-Penciolelli *et al.*, 1994
B27	Vpr	31–39	VRHFPRIWL	Addo & Rathod, 2004
B*2703 (B27)	p24	131–140	RRWIQLGLQK	Rowland-Jones *et al.*, 1998; Rowland-Jones, 1999
B*2705 (B27)			12 C	Jardetzky *et al.*, 1991; Rammensee *et al.*, 1995
			R L	
			F	
			K K	
			R R	
			G I	
			A	
B*2705 (B27)	p17	19–27	IRLRPGGKK	McKinney *et al.*, 1999; Lewinsohn, 1999
B*2705 (B27)	p24	131–140	KRWIILGLNK	Nixon *et al.*, 1988; Buseyne *et al.*, 1993; Goulder *et al.*, 1997c
B*2705 (B27)	gp160	786–795	GRRGWEALKY	Lieberman *et al.*, 1992; Lieberman, 1999
B*2705 (B27)	Nef	105–114	RRQDILDLWI	Goulder *et al.*, 1997b

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*3501 (B35)			2 C **P Y** A F V M S L I	Hill *et al.*, 1992; Rammensee *et al.*, 1999
B*3501 (B35)	p17	36–44	WASRELERF	Goulder *et al.*, 1997a
B*3501 (B35)	p17	124–132	NSSKVSQNY	Rowland-Jones *et al.*, 1995
B*3501 (B35)	p24	122–130	PPIPVGDIY	Rowland-Jones *et al.*, 1995
B*3501 (B35)	p24	122–130	NPVPVGNIY	Rowland-Jones *et al.*, 1995
B*3501 (B35)	RT	107–115	TVLDVGDAY	Wilkes & Ruhl, 1999; Wilson *et al.*, 1999
B*3501 (B35)	RT	118–127	VPLDEDFRKY	Sipsas *et al.*, 1997; Shiga *et al.*, 1996
B*3501 (B35)	RT	175–183	NPDIVIYQY	Sipsas *et al.*, 1997; Shiga *et al.*, 1996
B*3501 (B35)	RT	175–183	HPDIVIYQY	Rowland-Jones *et al.*, 1995
B*3501 (B35)	gp160	42–52	VPVWKEATTTL	Wilkes & Ruhl, 1999
B*3501 (B35)	gp160	78–86	DPNPQEVVL	Shiga *et al.*, 1996
B*3501 (B35)	gp160	606–614	TAVPWNASW	Johnson *et al.*, 1994
B*3501 (B35)	Nef	74–81	VPLRPMTY	Culmann *et al.*, 1991; Culmann-Penciolelli *et al.*, 1994
B*3701 (B37)			2 C **D F** **E M** **L** **I**	Falk *et al.*, 1993
B*3701 (B37)	Nef	120–128	YFPDWQNYT	Culmann *et al.*, 1991; Culmann, 1999
B*3801 (B38)	Vif	79–87	WHLGQGVSI	Sabbaj *et al.*, 2004
B*3801 (B38)	gp160	104–112	MHEDIISLW	Cao, 2002
B*3901 (B39)			2 C **R L** **H**	Falk *et al.*, 1995a
B*3901 (B39)	p24	61–69	GHQAAMQML	Kurane & West, 1999
B*3910 (B39)	p24	48–56	TPQDLNTML	Honeyborne & Kiepiela, 2005
B*4001 (B60)			2 C **E L**	Falk *et al.*, 1995b
B*4001 (B60)	p17	92–101	IEIKDTKEAL	Altfeld *et al.*, 2000
B*4001 (B60)	p24	44–52	SEGATPQDL	Altfeld *et al.*, 2000
B*4001 (B60)	p2p7p1p6	118–126	KELYPLTSL	Yu *et al.*, 2002b
B*4001 (B60)	RT	5–12	IETVPVKL	Draenert, 2004
B*4001 (B60)	RT	202–210	IEELRQHLL	Altfeld *et al.*, 2000
B*4001 (B60)	gp160	805–814	QELKNSAVSL	Altfeld *et al.*, 2000
B*4001 (B60)	Nef	37–45	LEKHGAITS	Draenert, 2004
B*4001 (B60)	Nef	92–100	KEKGGLEGL	Altfeld *et al.*, 2000

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*4002 (B61)	p17	11–19	GELDRWEKI	Sabbaj *et al.*, 2003
B*4002 (B61)	p24	70–78	KETINEEAA	Sabbaj *et al.*, 2003
B*4002 (B61)	p24	78–86	AEWDRVHPV	Sabbaj *et al.*, 2003
B*4002 (B61)	p2p7p1p6	64–71	TERQANFL	Sabbaj *et al.*, 2003
B*4002 (B61)	Nef	92–100	KEKGGLEGL	Sabbaj *et al.*, 2003; Altfeld *et al.*, 2000
B42	Integrase	260–268	VPRRKAKII	Kiepiela & Goulder, 2002
B*4201 (B42)	p24	48–56	TPQDLNTML	Goulder *et al.*, 2000a
B*4201 (B42)	RT	271–279	YPGIKVRQL	Wilkes & Ruhl, 1999
B*4201 (B42)	Nef	128–137	TPGPGVRYPL	Goulder, 1999
B44	Protease	34–42	EEMNLPGRW	Rodriguez *et al.*, 2004
B*4402 (B44)			2 C **E** **F** **Y**	Rammensee *et al.*, 1999
B*4402 (B44)	p24	162–172	RDYVDRFYKTL	Ogg *et al.*, 1998
B*4402 (B44)	p24	174–184	AEQASQDVKNW	Lewinsohn, 1999
B*4402 (B44)	gp160	31–40	AENLWVTVYY	Borrow *et al.*, 1997
B*4403 (B44)	p17	78–86	LYNTVATLY	Masemola *et al.*, 2004
B*4415 (B12)	p24	28–36	EEKAFSPEV	Bird *et al.*, 2002
B*4501 (B45)	p2p7p1p6	1–10	AEAMSQVTNS	Sabbaj *et al.*, 2004
B50	Nef	37–45	LEKHGAITS	Draenert, 2004
B51	Vif	57–66	IPLGDAKLII	Bansal *et al.*, 2004
B51	Vpr	29–37	EAVRHFPRI	Cao *et al.*, 2003
B*5101 (B51)			2 C **A** **F** **P** **I** **G**	Falk *et al.*, 1995a
B*5101 (B51)	RT	42–50	EKEGKISKI	Haas *et al.*, 1998; Haas, 1999
B*5101 (B51)	RT	128–135	TAFTIPSI	Sipsas *et al.*, 1997
B*5101 (B51)	gp160	416–424	LPCRIKQII	Tomiyama *et al.*, 1999
B*5201 (B52)			2 C **I** **V** Q	Rammensee *et al.*, 1999
B*5201 (B52)	p24	143–150	RMYSPTSI	Wilkes & Ruhl, 1999; Wilson *et al.*, 1997

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B53	Nef	135–143	YPLTFGWCF	Kiepiela & Goulder, 2002
B*5301 (B53)			2 C **P** **L**	Hill *et al.*, 1992
B*5301 (B53)	p24	48–56	TPYDINQML	Gotch *et al.*, 1993
B*5301 (B53)	p24	176–184	QASQEVKNW	Buseyne *et al.*, 1996, 1997; Buseyne, 1999
B*5301 (B53)	Tat	2–11	EPVDPRLEPW	Addo *et al.*, 2001
B*5301 (B53)	Nef	135–143	YPLTFGWCY	Sabbaj *et al.*, 2003
B*5501 (B55)			2 C **P** A	Barber *et al.*, 1995
B*5501 (B55)	gp160	42–51	VPVWKEATTT	Shankar *et al.*, 1996; Lieberman, 1999
B57	p24	32–40	FSPEVIPMF	Frahm *et al.*, 2005a
B57	Protease	70–77	KAIGTVLV	Frahm *et al.*, 2005a
B57	Integrase	123–132	STTVKAACWW	Rodriguez *et al.*, 2004; Addo & Rathod, 2004
B57	Nef	116–124	HTQGYFPDW	Draenert, 2002
B57	Nef	127–135	YTPGPGIRY	Frahm *et al.*, 2005a
B57	Nef	137–145	LTFGWCFKL	Frahm *et al.*, 2005a
B*5701 (B57)			12 C **A** **F** **T** **W** **S** K Y	Barber *et al.*, 1997
B*5701 (B57)	p24	15–23	ISPRTLNAW	Johnson *et al.*, 1991; Goulder *et al.*, 1996b
B*5701 (B57)	p24	30–40	KAFSPEVIPMF	Goulder *et al.*, 1996b
B*5701 (B57)	p24	108–118	TSTLQEQIGWF	Goulder *et al.*, 1996b
B*5701 (B57)	p24	176–184	QASQEVKNW	Goulder *et al.*, 1996b
B*5701 (B57)	RT	244–252	IVLPEKDSW	van der Burg *et al.*, 1997; Hay, 1999
B*5701 (B57)	Integrase	173–181	KTAVQMAVF	Goulder *et al.*, 1996b; Hay, 1999
B*5701 (B57)	Vpr	30–38	AVRHFPRIW	Altfeld *et al.*, 2001a
B*5701 (B57)	Vif	31–39	ISKKAKGWF	Altfeld *et al.*, 2001a
B*5701 (B57)	Rev	14–23	KAVRLIKFLY	Addo *et al.*, 2001
B*5701 (B57)	Nef	116–125	HTQGYFPDWQ	Culmann *et al.*, 1991
B*5701 (B57)	Nef	120–128	YFPDWQNYT	Culmann *et al.*, 1991
B*5703 (B57)	p24	30–37	KAFSPEVI	Goulder *et al.*, 2000b
B*5703 (B57)	p24	30–40	KAFSPEVIPMF	Goulder *et al.*, 2000b
B58	p17	76–86	RSLYNTVATLY	Frahm *et al.*, 2005a
B58	Tat	2–11	EPVDPRLEPW	Frahm & Brander, 2005

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*5801 (B58)			12 C **A** **F** **T** **W** **S** K V I	Barber *et al.*, 1997; Falk *et al.*, 1995b
B*5801 (B58)	p24	108–117	TSTVEEQQIW	Bertoletti *et al.*, 1998
B*5801 (B58)	p24	108–117	TSTLQEQIGW	Goulder *et al.*, 1996b
B*5801 (B58)	RT	375–383	IAMESIVIW	Kiepiela & Goulder, 2002
B*5801 (B58)	Rev	14–23	KAVRLIKFLY	Addo *et al.*, 2001
B62	Nef	19–27	RMRRAEPAA	Cao, 2002
B63	p17	76–86	RSLYNTVATLY	Frahm *et al.*, 2005a
B63	p24	15–23	ISPRTLNAW	Frahm *et al.*, 2005a
B63	p24	30–40	KAFSPEVIPMF	Frahm *et al.*, 2005a
B63	Rev	14–23	KAVRLIKFLY	Frahm *et al.*, 2005a
B63	Nef	127–135	YTPGPGIRY	Frahm *et al.*, 2005a
B63	Nef	137–145	LTFGWCFKL	Frahm *et al.*, 2005a
B81	Pol	715–723	LFLDGIDKA	Addo, 2002
B*8101 (B81)	p24	48–56	TPQDLNTML	Goulder *et al.*, 2000a
B*8101 (B81)	Vpr	34–42	FPRIWLHGL	Altfeld *et al.*, 2001a

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
Cw*0102 (Cw1)			23 C **A L** **L** P	Barber *et al.*, 1997
Cw*0102 (Cw1)	p24	36–43	VIPMFSAL	Goulder *et al.*, 1997a
Cw3	Nef	83–91	AALDLSHFL	Draenert, 2004
Cw*0303 (Cw9)	p24	164–172	YVDRFFKTL	Honeyborne, 2003
Cw*0304 (Cw10)	p24	164–172	YVDRFFKTL	Honeyborne, 2003
Cw*0304 (Cw10)	gp41	46–54	RAIEAQQHL	Currier *et al.*, 2002; Trocha, 2002
Cw*0401 (Cw4)			2 6 C **Y L** **P F** **F M** V I L	Falk *et al.*, 1994
Cw*0401 (Cw4)	gp160	375–383	SFNCGGEFF	Wilson *et al.*, 1997; Johnson *et al.*, 1993
Cw5	Gag p24	174–185	AEQASQEVKNWM	Draenert, 2004
Cw6	Nef	120–128	YFPDWQNYT	Frahm & Brander, 2005
Cw7	Nef	105–115	KRQEILDLWVY	Kiepiela & Goulder, 2002
Cw7	Nef	105–115	RRQDILDLWIY	Yu *et al.*, 2002a
Cw*0802 (Cw8)	p24	48–56	TPQDLNTML	Goulder *et al.*, 2000a; Honeyborne & Kiepiela, 2005
Cw*0802 (Cw8)	Nef	83–91	AAVDLSHFL	Cao *et al.*, 2003
Cw*0804 (Cw8)	p17	33–31	HLVWASREL	Masemola *et al.*, 2004
Cw12	Tat	30–37	CCFHCQVC	Cao *et al.*, 2003; Nixon *et al.*, 1999
Cw14	p17	78–85	LYNTVATL	Horton & Havenar-Daughton, 2005
Cw15	gp41	46–54	RAIEAQQHL	Trocha, 2002
Cw18	p24	161–169	FRDYVDRFF	Honeyborne & Kiepiela, 2005
Cw*1801 (Cw18)	Integrase	165–172	VRDQAEHL	Rathod & Kiepiela, 2005

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We very much welcome any criticism, comments and additions to this list since we are sure that some epitopes will unintentionally escape our attention, despite close monitoring of the literature. Please write or call us with any comments you may have at:

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I-B

Acute HIV Infection: Implications for HIV Spread, Disease Progression, and Vaccine Development

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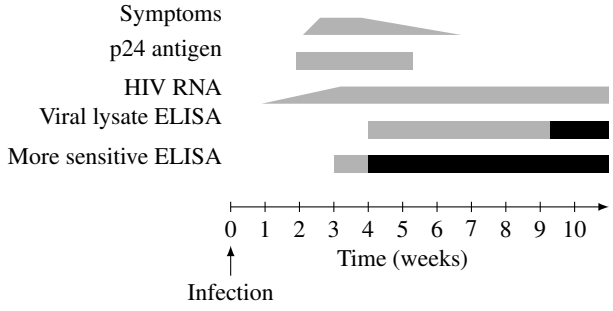
I-B-1 Acute HIV infection and its detection

The natural history of initial HIV infection can be arbitrarily divided into phases that include acute HIV infection, the first stage of disease (when HIV RNA can be detected in blood) before most HIV-specific antibodies form; recent or early infection, when antibodies in reduced concentration or reduced avidity can be detected; and established chronic HIV infection (Figure I-B.1 [Fiebig *et al.*, 2003; Pilcher *et al.*, 2004a]). Finding patients before seroconversion is critical to understand the HIV transmission event(s) effects and the effect(s) of host defenses on the viral population.

Figure I-B.1: Acute/early HIV infection timeline.



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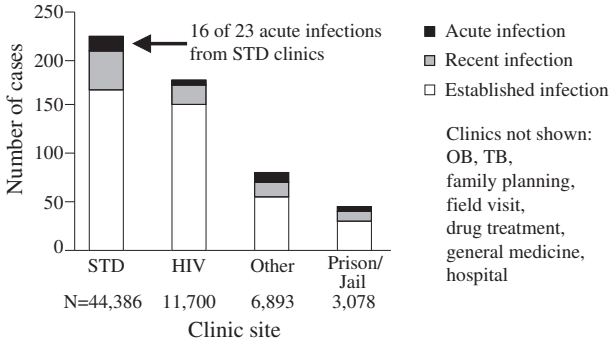
It is generally believed that half or more of patients with acute or early HIV infection may develop a "mono-like illness" [Schacker *et al.*, 1996; Lavreys *et al.*, 2000; Pilcher *et al.*, 2005]. Patients with acute HIV can present either for acute symptomatic care [Schacker *et al.*, 1996], for care of sexually transmitted disease (STD) symptoms [Pilcher *et al.*, 2005], or (realizing their elevated risk) for HIV testing. Although the diagnosis is rarely considered in acute patient care or testing settings, the potential for diagnosis is clearly present. For example, Rosenberg *et al.* [1999] reported that 1.0% of patients with negative tests for EBV (Epstein-Barr virus) infectious mononucleosis had serology consistent with acute HIV infection, and Pincus *et al.* [2003] found that 1.0% of patients with "any viral symptoms" in a Boston urgent care center had unsuspected acute HIV infection. However, searching for symptomatic subjects is a relatively inefficient strategy to detect subjects with acute or early HIV infection. For example, Rosenberg *et al.* found only about 150 subjects over 8 years [Kassutto *et al.*, 2005].

Alternative approaches involve "building a cohort" or longitudinal evaluation. The cohort approach requires enrollment of high risk, HIV seronegative subjects. For example, Lavreys *et al.* [2000] followed 883 female sex workers for up to five years at three month intervals. A total of 103 seroconversion events were observed. Fever, vomiting, diarrhea, headache, joint pain, body aches, skin rash, lymphadenopathy, fatigue and pharyngitis were more common among women who seroconverted. However, these patients were virtually all beyond the acute (antibody negative) phase of infection at the time of study.

Cross-sectional studies appear to offer the best strategy to find subjects before seroconversion. This approach was developed to make the blood supply safe, albeit at considerable cost [Ruiz *et al.*, 2001]. Recognizing that traditional antibody tests would inevitably miss some donors, blood banks in the United States and many other countries chose to eliminate infected (seronegative units) units with detection of HIV RNA [Engelfriet & Reesink, 2002; Roth & Seifried, 2002; Fang *et al.*, 2003; Mine *et al.*, 2003; Fiebig *et al.*, 2003; Koppelman *et al.*, 2005]. Bollinger *et al.* [1997] studied seronegative HIV in high risk sub-

jects in India. Among 6,495 consecutive attendees at two STD clinics in Pune, p24 antigen was detected in 58/3,874 (1.5%) of HIV seronegative samples. The majority of subjects with acute infection (51/58) were men. A group of 290 controls were matched on age and gender and compared for clinical signs of acute HIV infection. The most common symptoms associated with p24 antigenemia were fever, joint pain, inguinal lymphadenopathy, and night sweats; at least one of these symptoms was found in 47% of those with acute HIV infection.

Figure I-B.2: HIV-1 infections by testing site.

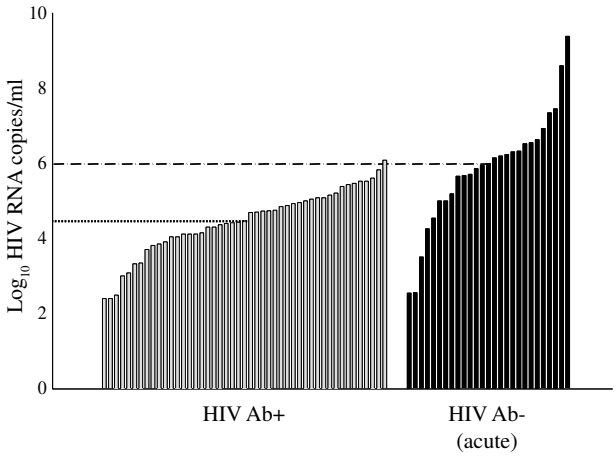


A series of studies have been completed that are designed to detect HIV RNA in blood in a large number of samples, using a serum pooling strategy adapted from the blood banking industry [Pilcher *et al.*, 2002, 2004b, 2005]. In North Carolina nearly 110,000 people seeking HIV testing were studied [Pilcher *et al.*, 2005]. A total of 563 people with established HIV infection were identified. A "detuned" ELISA assay designed to detect newly formed antibodies suggested 103 recent infections in the group of 563. Among HIV antibody negative specimens, 23 with HIV RNA (i.e., acute HIV infection) were detected. As shown in Figure I-B.2 most subjects with acute infection were detected in STD clinics. The median blood viral burden of subjects with acute HIV infection was 209,000 copies/ml, ten times greater than subjects with established infection.

These findings have led to increased focus on STD clinic subjects in developing countries [Pilcher *et al.*, 2004b]. As shown in Figure I-B.3, a group of 1360 men in an STD clinic in Lilongwe, Malawi were studied, and a total of 553 (40.6%) were HIV antibody positive. Analysis of HIV antibody negative specimens revealed that 24 men (1.8%) had unrecognized acute HIV infection, which represented 5.0% of all HIV infections detected. The factor most strongly associated with detection of acute HIV was attendance in the STD clinic [OR: 15.2 (95% CI: 2.04, 113.0)]. Patients with acute HIV infection had median blood viral burden > 10^6 copies/ml, significantly higher than the 10^4.5 copies/ml median observed in chronic infections (Figure I-B.3).

These results have recently been confirmed [Fiscus *et al.*,

Figure I-B.3: Viral load in Malawi: chronic and acute HIV infection



2005]. Among 1440 men and women studied in Malawi, 8% had established HIV infection and 1% (22 subjects) had acute infection. A heat-dissociated p24 antigen ELISA (see below) discerned 84% of the subjects with acute HIV infection. Of 1906 consecutive clinic attendees (47% female) recruited in the Hillbrow, Esselen Street STD Clinic in Johannesburg, SA, from April through October 2004 [Stevens *et al.*, 2005], a total of 672 individuals were HIV antibody positive (35.2%). In addition, 12 subjects (1% of antibody negative subjects) were HIV RNA positive (with acute HIV infection).

I-B-2 The importance of acute HIV infection

Detection of subjects with acute HIV infection raises three related concerns: i) implications for HIV surveillance; ii) opportunities to change the natural history of the disease; iii) opportunities for prevention of transmission.

Implications for HIV surveillance

Established HIV infection is detected by antibody testing. In recent years a variety of assays have been developed to detect antibodies with reduced concentration or avidity that are believed to reflect early (incident) infection [Janssen *et al.*, 1998; Brust *et al.*, 2000; Stramer *et al.*, 2000; Glynn *et al.*, 2000; Chen *et al.*, 2002; Stramer *et al.*, 2004]. The precise relationship between the time of infection and the veracity of these assays is difficult to assure, but current evidence suggests that positive results are obtained for at least several months after infection. Obviously, acute (truly incident) infections are not detected with antibody testing so the results of the cross-sectional methods applied to the general population are complementary, and can be quite

important if a substantial number of subjects are identified [Pilcher *et al.*, 2005].

Implications for treatment

The earliest stages of HIV infection reflect a battle between viral replication and emerging host defenses. The magnitude of the viral burden when the "set point" is reached will help to determine the natural history of the diseases [Mellors *et al.*, 1996]. In addition, results from animals and humans demonstrate considerable destruction of gut lymphoid cells during the earliest weeks of HIV infection [Lifson *et al.*, 2003; Guadalupe *et al.*, 2003; Brenchley *et al.*, 2004]. Accordingly, there has been great interest in early treatment of HIV. However, to date no sustained benefit of such therapy has been observed [Klein, 2001; Gegeny, 2002; Clements *et al.*, 2003; Kaufmann *et al.*, 2004; Di Mascio *et al.*, 2004; Smith *et al.*, 2004; Hammer, 2005]. Newer trials are focused on patients with acute or very early infection, and the concomitant application of antiviral drugs and agents that affect the cell cycle and/or state of cellular activation.

Implications for transmission prevention

The efficiency of HIV transmission depends on the viral burden [Quinn *et al.*, 2000] and the viral phenotype. The great viral burden characteristic of acute HIV infection virtually assures increased transmission risk [Pilcher *et al.*, 2004c]. In addition, many people with acute HIV infection have untreated STDs [Pilcher *et al.*, 2004b] which further increase genital tract viral shedding [Cohen *et al.*, 1997]. Mathematical modeling exercises have predicted that subjects with acute infection could play a disproportionate role in the epidemic. Jacquez *et al.* [1994]; Koopman *et al.* [1997] and recent analysis of data from Uganda [Koopman *et al.*, 1997] provide compelling support for this idea. Wawer *et al.* [2005] estimated the probability of HIV transmission from a subject with "early infection" (measured an average of 2.5 months after seroconversion) as 8.2/1000 episodes of intercourse, with established infection as 7–15/10,000, and with advanced (unrestrained and untreated) infection as 2.8/1000. The authors estimated that 43% of new HIV infections observed in their study population could be ascribed to subjects with acute and early infections.

I-B-3 Clades and transmission

The viral burden represents only a part of the story. The genotype and phenotype of the viral population must also play a crucial, albeit poorly understood role.

A key feature of HIV-1 is its genetic heterogeneity represented by distinct subtypes (A-K) [von Briesen *et al.*, 1990; Leitner *et al.*, 2004]. The HIV-1 clades or subtypes are not equally distributed around the globe, with subtype C representing approximately one-half of all infections. The existence of these phylogenetic clades likely represents an early isolation or bottleneck to establish subepidemics out of a more diverse initial epidemic. In areas of cocirculating subtypes, recombinants are common, suggesting there is no genetic barrier that has isolated the subtypes. There has been widespread interest in the possibility that the subtypes have different biological properties. A study by Devito *et al.* [2002] suggests a differential response in neutralizing antibodies in seronegative individuals exposed to clades A and D vs. clade B. IgA purified from the blood and genital tract from sex workers from Nairobi and Kenya, wherein clades A and D predominate, demonstrated significant cross-clade HIV-1 neutralization. In contrast, a more clade-specific pattern of neutralization was found in noninfected sex partners of clade B individuals. In addition, one study that indicated subtype C isolates have reduced replicative capacity in cell culture relative to subtype B isolates [Ball *et al.*, 2003] runs counter to the world-wide success of the subtype C virus, suggesting simple correlations between *in vitro* measures of biology and subtypes may be problematic.

One difference that has been widely reported is that subtype C HIV-1 appears to be less likely to undergo a coreceptor switch from using CCR5 to using CXCR4 [Tscherning *et al.*, 1998; Abebe *et al.*, 1999; Bjorndal *et al.*, 1999; Ping *et al.*, 1999; Cecilia *et al.*, 2000; Morris *et al.*, 2001]. Since most transmission events involve an R5 virus, this might suggest subtype C HIV-1 has an advantage in the rate of transmission over subtypes that could have their R5 pool diluted with X4 viruses. However, the site of the block of transmission of X4 viruses is not known, if indeed there is one, so that the potential impact of this subtype difference is hard to evaluate.

Others postulate that HIV-1 clade C could theoretically be more genetically fit than other clades due to an increased number of NFκB sites (up to 3 in clade C) within the long terminal repeat which could enhance proviral DNA transcription [Montano *et al.*, 2000]. More direct indications of potential differences between subtypes are suggested by the detection of subtype C viral sequences, but not subtype A viral sequences, in vaginal secretions of a person coinfected with subtype C and subtype A viruses [Iversen *et al.*, 2005] and higher rates of vertical transmission of subtype C HIV-1 compared to subtypes A or D [Renjufi *et al.*, 2004], as well as higher rates of nevirapine resistance in women with subtype C vs. A or D after treatment with single-dose nevirapine [Eshelman *et al.*, 2005]. Taken together, these data suggest that different HIV clades may alter disease progression and pathogenesis.

I-B-4 The transmitted swarm

HIV-1 exists as a complex mixture of genotypic variants within an infected person. This complexity can be used to estimate the extent of the bottleneck that occurs during transmission. Early reports were conflicting as to whether the transmitted virus was homogeneous [Amedee *et al.*, 1995; Delwart *et al.*, 1994; Furuta *et al.*, 1994; Kliks *et al.*, 2000; McNearney *et al.*, 1993; Mulder-Kampinga *et al.*, 1993; Ou *et al.*, 1992; Pang *et al.*, 1992; Shankarappa *et al.*, 1999; Sodora *et al.*, 1998; Wolfs *et al.*, 1992; Zhu *et al.*, 1993], suggesting a strong bottleneck; or heterogeneous [Delwart *et al.*, 1997; Dickover *et al.*, 2001; Enose *et al.*, 1997; Kampinga *et al.*, 1997; Lamers *et al.*, 1993; Learn *et al.*, 2002; Liu *et al.*, 1997; Nowak *et al.*, 2002; Pilcher *et al.*, 2001; Scarlatti *et al.*, 1993; Sutthent *et al.*, 1998; Verhofstede *et al.*, 2003; Wolinsky *et al.*, 1996; Zhu *et al.*, 1996], suggesting the transmission of multiple variants [Rademeyer *et al.*, 2004; Ritola *et al.*, 2004].

Interest in this area was renewed with the report that with heterosexual transmission women are frequently infected with multiple variants while men are typically infected with a single variant [Long *et al.*, 2000]. This study was extended to detect transmission of multiple variants for several other subtypes, although in smaller studies [Sagar *et al.*, 2003]. Moreover, genital tract infections have been estimated to increase the risk of acquiring multiple vs. single variants nearly five fold in women [Sagar *et al.*, 2004], possibly secondary to transmission of cell-associated virus with multiple proviruses. The detection of single variants in men was reported but in a cohort where the risk factor was not known [Delwart *et al.*, 2002]. Conversely, multiple variants were detected early after transmission in a homosexual male cohort but these variants became more homogeneous in the subsequent weeks [Learn *et al.*, 2002].

Finally, we have detected multiple variants in half of the men infected through homosexual exposure, suggesting that this mode of transmission may be more similar to the risk of women in heterosexual exposure than of men in heterosexual exposure [Ritola *et al.*, 2004]. The question of the number of transmitted variants is important to resolve for two reasons. First, the transmission of multiple variants is inconsistent with transmission being infrequent and a virus particle being the minimal infectious unit, suggesting fundamental features of the mechanism of transmission remain unknown. Second, longitudinal follow-up of women infected with single versus multiple variants showed that infection with multiple variants was associated with more rapid progression [Sagar *et al.*, 2003]. Thus, features of virus transmission and the impact of this earliest event in infection on the entire disease course remain important areas of study.

I-B-5 Features of the transmitted virus

A long-standing interest in the vaccine field has been to understand the nature of the transmitted virus as this is ultimately the entity that a vaccine must protect against. The null hypothesis is that the transmitted variant is simply a randomly selected subset of the total virus population in the donor. However, compartmentalization of the virus population in the genital tract secretions that carry the transmitted virus or early selection for specific variants in the newly infected recipient could alter the composition of the virus population in ways that might impact vaccine design.

Derdeyn *et al.* [2004] have reported that subtype C HIV-1 isolated from newly infected subjects in a discordant couple cohort have env genes that are largely homogeneous, encode Env proteins that are more neutralization sensitive than the Env proteins of the donor virus, and have shorter variable loop lengths in Env compared to the circulating virus in the donor. The hypothesis to explain these observations is that the recipient initially represents an antibody-negative environment that rapidly selects for variants that can grow more rapidly but at the expense of having an Env protein that is more neutralization sensitive.

Similar reduced V1/V2 loop length and reduced number of glycosylation sites were observed in heterosexual transmission of subtype A HIV-1 [Chohan *et al.*, 2005]. However, no such differences in neutralization sensitivity, variable loop length, or glycosylation site number have been seen for (largely homosexual) transmission of subtype B HIV-1 [Chohan *et al.*, 2005; Frost *et al.*, 2005]. It is not obvious how different subtypes or different modes of transmission could have such a dramatic impact on determining the nature of the transmitted variant. At present these questions remain unresolved yet relevant to our understanding of HIV transmission and early infection.

I-B-6 HIV compartmentalization and implications for transmission

Substantial research has focused on HIV-1 variation within anatomical compartments in acute and chronic HIV-1 infection; compartmentalization can occur in a variety of areas including plasma, brain, genital tract secretions, or within different leukocyte compartments [Zhu *et al.*, 1996; Eron *et al.*, 1998; Staprans *et al.*, 1999; Kiessling *et al.*, 1998; Haddad *et al.*, 2000; Gupta *et al.*, 2000; Venturi *et al.*, 2000; Pilcher *et al.*, 2001; Poles *et al.*, 2001; Sutthent *et al.*, 2001; Zhang *et al.*, 2002; Potter *et al.*, 2003; Kemal *et al.*, 2003; Tirado *et al.*, 2004; Ghosn *et al.*, 2004; Potter *et al.*, 2004; Philpott *et al.*, 2005; Ritola *et al.*, 2005; Smit *et al.*, 2004; Sullivan *et al.*, 2005; Adal *et al.*, 2005]. One of the first examinations of viral compartmentalization was done by Zhu *et al.* [1996], and examined envelope gp120 se-

quences in plasma and genital secretions of patients acutely infected with HIV-1, and their chronically-infected sexual partners. Envelope sequences from the acutely infected group were largely homogeneous, and represented a minor variant of the population found in the semen of the transmitting partner. These data provided the first evidence that HIV-1 selection may occur during sexual transmission. Further analysis of envelope gp120 sequences during acute infection revealed that variants transmitted during acute infection form the genetic basis for subsequent viral diversification that leads to heterogeneity in chronic infection [Zhang *et al.*, 2002]. Kemal *et al.* [2003] found that in a majority of women, gp120 sequences from the genital tract and plasma are distinct. Envelope gp120 glycosylation sites, which are hypothesized to form a protective shield and facilitate neutralization escape, were significantly different between the two compartments.

These studies suggest that compartmentalization observed in chronic infection is likely secondary to gradual viral evolution from a dominant species, rather than differential migration of variants to various anatomical locations during acute infection. To analyze the dissemination of HIV-1 into various anatomical compartments during primary infection, including plasma, cerebrospinal fluid (CFS), semen, cervicovaginal lavage fluid, and/or saliva in 17 individuals, Pilcher *et al.* [2001] confirmed that viral dissemination is highly efficient and dynamic, and concluded that antiretroviral therapy is unlikely to limit initial virus spread to most tissue compartments, although it may reduce genital tract shedding and central nervous system (CNS) expansion. In those subjects that are infected with multiple variants, these variants appear to penetrate the seminal compartment and CNS (CSF) equivalently [Ritola *et al.*, 2004].

In addition, there is growing evidence that the genital tract of both males and females can serve as a reservoir for drug resistance mutations: paired analyses of plasma and genital secretions in nine of twelve women exhibited different drug-resistance mutations [Tirado *et al.*, 2004]. A similar result was obtained in men, wherein the rate and pattern of emergence of resistance varied between plasma and semen [Eron *et al.*, 1998]. Additional phylogenetic analyses of clones of the HIV pro gene have revealed variants in semen that originate not only from passive diffusion from blood, but also from local production within semen [Ghosn *et al.*, 2004]. Additional studies to analyze the interplay between cellular, humoral, and viral factors involved in drug resistance and compartmentalization are critical to HIV pathophysiology and controlling the infection.

I-B-7 Resistance characteristics of the transmitted virus

Although highly active antiretroviral therapy (HAART) has significantly decreased morbidity and mortality from HIV, treatment remains problematic due to the development of resistance to antivirals and evasion of the host immune system. Blower *et al.* [2001] have identified several factors that may enhance the transmission of resistant virus: an increasing proportion of HIV-infected patients who are on antiviral therapy (increased probability of acquiring infection from treated person), an increasing rate at which patients on antiviral treatment develop drug resistance (dependent on potency, adherence, genetic barriers), an increasing relative fitness of the resistant strains (dependent on replicative capacity of the resistant strain), a decreased transmissibility of drug-sensitive strains from treated patients, and individual risk factors.

Surveillance of the transmitted variants is crucial to understanding these factors, rational drug use and vaccine development. Indeed, transmission of drug-resistant viruses has been the subject of intense scrutiny in the recent past and remains a significant public health concern. A series of prevalence reports from North America and Europe indicate the transmission of HIV-1 resistance is steadfastly increasing [Salomon *et al.*, 2000; Grant *et al.*, 2002; de Mendoza *et al.*, 2005; Yerly *et al.*, 2001; Little *et al.*, 2002] with measurements ranging from 3% to 23% for one or more drugs. Differences are at least in part due to study design, number of patients, resistance testing, definitions of resistance, geography, variability in antiviral selection, timeline, and risk factors for transmission. Although multiple studies have confirmed the increasing frequency of transmission of drug-resistant virus, these estimates may be an underestimate as the sequencing techniques for genotypic analysis did not quantify minor populations below 25%. To determine the prevalence of these minor variants, Metzner *et al.* [2005] have devised a quantitative real-time PCR assay using allele-discriminating oligonucleotides for three key resistance mutations, L90M (protease), K103N and M184V (RT). In 49 acute seroconverters in Germany from 1999 to 2003, overall drug resistant variants were detected in 20.4%. The L90M, K103N, and M184V were found in 2%, 10%, and 12%, respectively. Thus, knowledge of the prevalence of major and minor resistance variants may impact antiretroviral therapy.

Transmission of drug resistance mutations has been shown to affect disease outcome and response to antiviral treatment. Little *et al.* [2002] found that among subjects infected with drug-resistant virus, there was a significant delay in viral suppression after initiation of antiretroviral therapy (median of 88 days vs. 56 days). Moreover, even though there was no significant difference in mean

baseline plasma viral loads between the susceptible and resistant cohorts, once suppression was achieved the time to virological failure was significantly shorter in the patients infected with resistant virus (approximately 80% vs. 40%, respectively, remaining suppressed 500 days after achieving viral suppression). These data indicate that antiretroviral therapy is twice as likely to fail in patients infected with drug-resistant virus. In addition, drug-resistant HIV-1 isolates have been shown to persist in the host after primary infection without reversion to wild-type, even in the absence of drug therapy [Barbour *et al.*, 2004; Brenner *et al.*, 2002; Chan *et al.*, 2003; Delaugerre *et al.*, 2004]. These data suggest that some drug-resistant mutants have altered genetic fitness. In addition, Turner *et al.* [2004] compared the incidence of HIV-1 variants containing resistance to thymidine analogues, RT inhibitors, and protease inhibitors in primary HIV and chronic HIV infection. M184V was found in early HIV infected patients significantly less than in the chronic (potential transmitter) HIV infected group, 10% vs. 70%, respectively. The reduced transmissibility of M184V in the potential transmitters may be secondary to reduced viremia (up to 0.8 log lower) or compartmentalization of variants lacking M184V.

I-B-8 Conclusions

Renewed interest has developed in acute and early infection in recent years. New strategies to identify subjects in acute infection in the course of standard HIV screening open the possibility of early intervention both to preserve immune function (early therapy) and to reduce transmission during this period of high infectiousness. Analysis of the transmitted virus has raised questions about the nature of the transmission event and about the earliest features of viral evolution with implications for vaccine design and disease progression. The study of acute infection will continue to extend our knowledge about the earliest response of the human host to the virus and its limitations that result in a failure to clear the virus. This knowledge will become the cornerstone of a new generation of vaccine strategies based on a deeper understanding of these earliest events of HIV-1 infection.

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I-C

Gateway to Tools of the HIV and HCV Databases

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I-C-1 Introduction

Over the years the staff of the HIV databases have developed web-based software for working with HIV sequence data. This is a general overview of the tools that are available on the HIV database website. Many of these tools are very simple, and were developed because we wanted to ease frequently-used computational tasks for our colleagues who use the database.

Some tools are tailored for HIV or HCV, and have counterparts developed specifically for the HCV (`http://hcv.lanl.gov/`) or HIV (`http://hiv.lanl.gov`) databases. Others are general and can be used for analysis of any organism. A fast way to understand what these programs do is to click the "Sample Input" button on the input page. This causes an example input file to be loaded into the input page, so you can run the program to get an idea about what the output looks like.

I-C-2 Outline of HIV database tools

This part of this publication provides an outline of these programs organized by their functions. A short description of each tool is provided. If a tool can be applied to any sequence, not just HIV or HCV, it is labeled, "General," while a tool that is applicable only to HIV or HCV sequences is labeled "HIV/HCV".

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Formats

Convert between formats

Format Converter Converts sequence files between 18 standard bioinformatics formats. Automatic recognition of input format. (General)

Seq-Convert Converts between 8 standard bioinformatics formats. No automatic recognition of input format. (General)

Formatting for publication

SeqPublish Formats an alignment for publication: identical columns are replaced by dashes, and the sequences are printed interleaved in blocks of user-determined length. (General)

Sequence and alignment manipulation

Translate Converts nucleotide sequences to 1-letter amino acid sequences. (General)

Gapstreeze (Gap strip/streeze) Removes columns containing more than a user-determined percentage of gaps. (General)

Consensus Builds consensus sequences of alignments according to user specifications. (General)

Generation of alignments

Gene Cutter Extracts coding regions from a nucleotide alignment, codon-aligns and translates them, highlighting frameshifts, stop codons, and translates alternatives from IUPAC ambiguity codes. (HIV/HCV)

SynchAligns Synchronizes two alignments that overlap so they are aligned to one another, optionally trimming alignments to the region of overlap. (General)

PrimAlign Retrieves an alignment of a nucleotide sequence fragment (e.g., a primer) from our HIV complete genome alignment to assess variability. (HIV/HCV)

Epilign Retrieves an alignment of a HIV-1 peptide, epitope or functional domain from our web protein alignments to assess variability. (HIV/HCV)

Sequence analysis

Sequence characterization

Sequence locator Determines the beginning and ending positions numbers of sequence fragments in the genome or proteome relative to database reference strains. (HIV/HCV)

HIV/HCV BLAST Finds sequences most similar to your query in the HIV database. Helpful in detecting possible contamination issues. (HIV/HCV)

Sequence subtyping and recombination

SUDI Determines if a newly discovered set of related sequences should be considered a new subtype, according to standards developed by the HIV nomenclature committee. (HIV specific)

RIP Identifies intersubtype recombination by calculating similarity in a sliding window between your query sequence and a set of HIV-1 reference sequences of different subtypes. (General)

CRF-DRAW Maps HIV-1 recombinant breakpoints onto a graphical figure of the HXB2 genome, with parental subtypes indicated by different colors. (HIV/HCV)

Sequence analysis

VESPA Identifies site-specific signature residues that are rare in one group of sequences and common in another and calculates the frequencies of different amino acids in each position. (General)

PCOORD Summarizes the variation in the sequences in 10 dimensions using principal coordinate analysis. (General)

Hypermut Tracks base substitution patterns, and highlights G→A substitution events relative to other mutations, as they dominate in sequences damaged by hypermutation. (General)

N-Glycosite Highlights and tallies potential N-linked glycosylation sites in a protein alignment. (General)

Entropy Quantifies variation in a given position in an alignment using Shannon Entropy, and statistically compare variation in each position in two sets of aligned sequences. (General)

SNAP Calculates synonymous/non-synonymous substitution rates for a set of codon-aligned nucleotide sequences, based on the method of Nei and Gojobori. (General)

ADRA Finds mutations associated with anti-HIV drug resistance in HIV-1 protease, RT, integrase, and envelope sequences. (HIV)

Phylogeny

Phylogenetic trees

TreeMaker Generates a neighbor joining tree which is displayed and downloadable. PHYLIP outfile and Newick-formatted treefiles can also be downloaded. (General)

Search HIV sequence DB and make a tree Combines your sequences with those obtained through a database search, aligns the combined set, and generates a tree. (HIV/HCV)

FindModel Analyzes your alignment to see which evolutionary model best describes the input sequences. Can be used to generate a better phylogenetic tree. (General)

Immunology

PeptGen Generates a set of overlapping peptides according to user specifications from a protein sequence or an alignment. (General)

ELF Identifies potential and known epitopes in immunologically reactive peptides using HLA anchor motifs. (HIV/HCV)

Motif Scan Finds HLA anchor residue motifs within protein sequences for specified HLA serotypes, genotypes or supertypes using two major motif libraries. (General)

Hepitopes Tests for HLA alleles that are enriched in individuals that react with a set of peptides. Useful for population studies. (General, although the output can be combined with ELF and tailored to HIV/HCV.)

Also see, Epilign and Sequence Locator, above, two tools originally developed for mapping epitopes and their diversity.

Database searches

We are listing the HIV/HCV search capabilities here, although they will not be described in detail in this review; a comprehensive review of the databases and search interfaces will be included in the 2006 compendium.

HIV Sequence Database

Website content Google search for content and topics anywhere on our website. Where: small search box at upper left on most pages.

Sequence databases Search for sequences by selecting from numerous criteria such as subtype, genomic region, sequence length, geographic origin, time from infection, etc. From the results page, sequences can be selected, downloaded, used to generate a phylogenetic tree, aligned, translated, etc.

Advanced Search Build your own search criteria by selecting from a more extensive list of search fields than is available on the standard search page.

Search/display by geography Maps geographic distribution of HIV-1 sequences and their subtypes and can be used for sequence retrieval.

Drug Resistance DB Search for mutations that confer resistance to HIV-1 drugs. Search fields include protein, drug class and compound, amino acid position, citation, etc.

HIV Molecular Immunology Database

Website content Google search for content and topics anywhere on our web site. Where: small search box at upper left on most pages.

CTL epitopes Search for known CTL or CD8+ epitopes by protein, sequence, immunogen, vaccines, HLA, author or keywords. Retrieves epitope summaries from the literature, alignments, Medline links and epitope maps.

T-helper epitopes Search for T-helper or CD4+ epitopes, analogous to the CTL database.

Antibodies Search for HIV antibodies by protein, sequence, immunogen, AB type, author, monoclonal antibody name or keywords.

Best-defined epitopes Search for the best-defined CD8+ T-cell epitopes by serotype, genotype or protein.

Vaccine trials Search data from published studies on SIV, HIV and SHIV vaccine trials in nonhuman primates. Search criteria include objective, species, publications, vaccine immunogen, adjuvant and challenge.

I-C-3 Detailed Descriptions of Tools

Seq-Convert—Format conversion

Purpose This interface combines four different sequence alignment format conversion tools.

Background Many tools on the website now are fairly good at automatically recognizing common sequence formats, but in some cases they fail and manual conversion is necessary, or a user may need to change their sequence format to make it compatible with another tool. Seq-Convert is a combination of

1. Seq-Convert, which in turn combines code from an extension of the READSEQ program developed by Don Gilbert [Gilbert] and code developed by the HIV database staff to produce the table, GDE and SLX output formats. The interface can read all formats it writes except for these three.
2. Omniread: This tools attempts to automatically recognize the format of your input file, using a different combination of the programs Fmtseq and Readseq.
3. cf: This tool, developed by Charles Calef at the HIV database, attempts to automatically recognize and convert a total of 18 sequence formats.
4. Readseq2: A web interface to the update of Readseq, Don Gilbert's sequence reformatting tool.

Sequence reformatting is a recurring and difficult problem. Many formats are only very loosely defined, while others are very strictly defined but difficult to parse. Our databases mostly use fasta and table format, but some 50 different formats are used in the sequencing world. The Seq-Convert suite combines enough programs that almost any sequences can be converted to something more common, but it may require some experimentation to find the right tool for unusual formats. The tool shows the resulting sequences, so the user can decide quickly if the conversion has succeeded or not.

History and context Seq-Convert is a combination of efforts of several people. Don Gilbert created the Readseq and Readseq2 programs. Brian Gaschen wrote the code for Seq-Convert, the least flexible but probably the most robust tool; Charles Calef wrote cf, which is very flexible but not extensively tested. Carla Kuiken created Omniread by testing the Readseq and Fmtseq input and output algorithms and combining the best of those. Anita Dalwani combined all tools in one website.

SeqPublish

Purpose Make visually attractive, publication-quality alignments.

Background This interface takes a sequence alignment and replaces residues identical to those in a reference sequence with dashes. Either the first sequence in the input alignment will be used as the reference sequence for the output, or you can create a consensus from the alignment to be used as the reference sequence. This program is useful for making publication quality figures, or for exploratory work that involves visually assessing levels of variation in a region. It can be used in conjunction with alignments created using the search interface.

History and context Implemented by Patrick Rose and Kristina Kommander; designed by Carla Kuiken.

Translate

Purpose This simple program translates nucleotide sequences to amino acids in frame 1 or all frames. Users who retrieve nucleotide alignments from our database but who are unfamiliar with multiple alignment programs can easily obtain an amino acid alignment.

History and context Suggested by a database user. Implemented on the web by Charles Calef using a translation subroutine by Brian Gaschen.

Gapstreeze—Gap Stripping and Squeezing

Purpose Remove columns of gaps from an alignment. Generally useful for preparation of alignments for phylogenetic analysis. Offers various options like removing only positions that contain more than a user-specified percentage of gaps.

Background HIVs and SIVs not only evolve by base substitution, but they also frequently mutate through insertions and deletions (indels), which tend to be imperfect direct repeats focused in hypervariable "hot spots". These regions can be difficult to align, and gaps must be included to compensate for insertions and deletions relative to other sequences in the alignment. While indels are often forced into the same positions in an alignment, it can be difficult to resolve whether they have evolved by base substitution, the baseline assumption of most phylogenetic tree programs, or by insertion and deletion. For example, a single insertion event of 15 bases might suggest unreasonably large evolutionary distances between two otherwise very closely related sequences. A blunt way to resolve this problem is to simply remove all positions from an alignment that have a gap inserted to maintain the alignment. Alignment programs generally use a tilde (~), or dash (-), to indicate a gap. Positions with missing information in some sequences will also be deleted, so the gene regions compared between all sequences will be the same. For this reason, users may want to remove particularly short sequences from an alignment before gap-stripping, as the alignment will only be as long as the shortest sequence included.

How to use Set the value of tolerance between 0% and 100%. A value of 0% will cause columns to be deleted if they contain any gaps (gapstrip), while a value of 100% will delete only columns that are entirely (100%) gaps (gapsqueeze). An intermediate tolerance value, of say, 10% will delete columns with more than 10% gap characters. You can define multiple gap characters and even specify ordinary letters to be gaps. This latter tactic is useful if, for example, you are interested in removing all columns containing IUPAC ambiguity codes (e.g. R and Y) from your nucleotide alignment, thereby preserving only columns with ATGCU. The "Show deleted columns" feature will include the intact first sequence in the output with marks showing columns that were deleted in the stripped alignment that follows. The default values set for the submission page will cause only columns that are 100% dash (-) characters to be removed.

History and context Many programs enable gap stripping, but Gapstreeze offers more flexibility with regard to specifying which columns are deleted, and retains a record of deleted columns. The record is particularly helpful if it is important that the alignment is codon aligned, as HIV sequences are often not biologically active and contain frameshift mutations. Any contiguous deleted columns that are not divisible by three would cause a frameshift downstream for the entire alignment. Brian Gaschen wrote the original script to facilitate preparing sequences for phylogenetic analysis, implementing features requested by Bette Korber; Charles Calef created an improved version and made a web interface.

Consensus Maker

Purpose Consensus Maker takes an input file of aligned sequences and calculates a consensus sequence for those sequences. Consensus sequences are useful as reference sequences for alignments or for reagent design.

How to use The consensus tools website offers three choices for creating a consensus of your alignment: simple, advanced, and ambiguity:

Simple consensus This option calculates a quick consensus of an alignment based on customary parameter choices.

Advanced consensus This option allows complete control over consensus parameters such as the values to be used for unanimity and majority, what characters to consider when making the consensus, whether to squeeze gaps, etc.

Ambiguity consensus A consensus sequence made up of the IUPAC ambiguity codes for each column in a nucleotide alignment can also be computed.

Example ambiguity consensus:

```
CON           AGCTRWMYSK HDBVNA
A.sequence1   AGCTAAACGG aagaAA
A.sequence2   AGCTAAACGG cgcgGA
A.sequence3   AGCTAAACGG tttcCA
A.sequence4   AGCTAAACGG tttcTA
B.sequence5   AGCtAAACGG tttcAA
B.sequence6   AGCtAAACGG tttcGA
B.sequence7   AGCtAAACGG tttcCA
B.sequence8   aGCtGTCTCT tttcTA
B.sequence9   aGCtGTCTCT tttcGA
B.sequence10 aGCtGTCTCT tttcTA
B.sequence11 #$*!?xxyyz zttcCA
```

Input options

Format of input alignment Consensus Maker recognizes most standard alignment formats.

Squeeze gaps If your alignment contains columns that are entirely gaps, they will be removed before a consensus is calculated. Default is squeeze gaps. You can also specify what character is used in your alignment to signify gaps. The default is -.

Output options

Do consensus for each block If the input contains blocks of sequences, such as subtypes, then calculate a consensus for each block, not just a single consensus for the alignment as a whole. Default is false.

Minimum number of sequences for a consensus If a block contains fewer than *n* sequences, then don't calculate a consensus for that block. Default is 3.

Do consensus of consensuses If consensuses are to be computed for each block in the alignment also calculate a consensus of these consensuses. (This would provide an HIV-1 M group consensus weighting all subtypes equally). Default is false.

Consensus + alignment Results will show consensus appended to the top of the user's alignment. Default is true. When false, the output consists of the consensus alone.

Output format A "pretty print" output shows your alignment aligned to the consensus with 50 characters per line and spaces every 10 characters.

Consensus calculation options

Unanimous value The fraction of characters in a column of the alignment needed to establish unanimity (shown as a capital letter) for that column. Default is 1.0.

Majority value The fraction of characters in a column of the alignment needed to establish majority (shown as a lowercase letter) for that column. Default is 0.5.

Use most common character This option determines what symbol to enter in the consensus for a column that has no majority character. Suppose a column contained letters AAAGGTTC. Does the user want that column to be represented in the consensus by a (i.e., the most common letter) or by ? (i.e., no letter forms a majority)? If so, then set this value to false. If multiple blocks are present in the alignment and there is a tie between two letters in one block, the program will try to resolve the tie by looking at that column of the alignment in all other blocks as well.

Characters to count when making consensus This is a set of characters ("letters") that the program considers when making a consensus. The default for nucleotide alignments is the set of valid nucleotide characters and the gap character ACGTU-. Using these defaults, the alignment column AAAAAXAA would have a consensus of A because the X character is ignored—it's not in the set of valid characters.

Use any character when making consensus Finally, if you want to consider *all* characters (including blanks, *, x, $, etc.) when making a consensus, check this box.

Options unique to ambiguity consensus

Characters to count when making consensus The program considers ACGTU when making a consensus.

Character presence percentage If a column of an alignment contained 99 A and 1 G would you want to give this a consensus of A or R, where R is the IUPAC code for purine (A or G)? In other words, if a character is present below a certain "presence percentage" threshold, should it be ignored when making the consensus? You can set this presence percentage threshold in the box provided. The default is 0, which means every occurrence of an A, C, G, T or U counts. If you had set the value to, say 2%, then the G in the above example would be ignored and the consensus would be A.

History and context We make alignments relative to consensus sequences to minimize the changes in the alignments and make it easier to see the differences between sequences. Consensus sequences also are central to circulating strains, and can be synthesized for vaccine design [Korber *et al.*, 2001; Gaschen *et al.*, 2002] or in reagent design (for example, HIV consensus sequence overlapping peptide sets for EliSpot [Korber *et al.*, 2001]). The tie-breaking algorithm and the concept of creating an HIV-1 M group consensus as the consensus of the subtype consensus sequences was developed by Bette Korber for reagent design. Charles Calef, with input from Carla Kuiken, developed this web-based tool to generate consensus sequences. Ready-made consensuses are available in our alignments section, useful in reagent design, and periodically updated.

Gene Cutter

Purpose Gene Cutter extracts pre-defined HIV-1 protein coding regions from a set of nucleotide sequences, then codon aligns and provides translations of the cut regions. It is particularly helpful for processing alignments of full-length HIV-1/SIVCPZ or HIV-2/SIVSMM genome sequences, or long interior regions that contain multiple coding regions.

Background All coding regions are clipped from a nucleotide alignment, and a matched codon-aligned nucleotide and translated protein alignment are created. Gene Cutter translates all codon possibilities in sequences containing IUPAC/IUB multistate characters, and provides a web-based format that allows users to move rapidly between nucleotide and protein alignments, and get details regarding translational properties of multistate characters. This tool is useful for sequence quality control of new sequences, as all stop codons and frameshifts are highlighted so potentially lethal mutations can be rapidly identified and cross-checked. Indels cause problems for multiple alignment programs, and often codons are split in an automated alignment and not readily translated; Gene Cutter will keep codons associated in the sequence. If a lethal frame shift occurs that is not compensated for within five

amino acids downstream, the codon is translated as a hash, (#), and the appropriate downstream translation of the sequence beyond the inactivating substitution is thus enabled. The protein translations Gene Cutter creates can also be helpful for generating GenBank submissions.

Input The input file can include either HIV-1 and SIVCPZ sequences or HIV-2, SIVsm and SIVmac, but these sets should not be mixed because of different gene boundaries. Gene Cutter is organism-specific and does not extend to all primate lentiviruses, just the two human HIV lineages and their most closely related SIVs. Sequences can either be aligned, in which case Gene Cutter will modify the alignment to make it codon aligned and split out each codon region, or unaligned, in which case Gene Cutter will create a baseline alignment. The unaligned input option takes longer to run.

Output The matched nucleotide and amino acid alignments can be saved to your computer for further study. Working with the output on the web interface enables rapid switching between DNA and protein alignments and identification of problematic frame shifts and stop codons. A nucleotide alignment could be opened in BioEdit, and the ability to move between nucleotide and protein alignments would be retained. We recommend reviewing your Gene Cutter alignment (or any automatically generated alignment) and hand editing as needed.

History and context Brian Gaschen first developed this tool for internal database work, in response to increasing acquisitions of large numbers of full-length sequences that needed rapid processing. He built the public web interface incorporating suggestions provided by local users Bette Korber, Thomas Leitner, as well as outside users Jean Carr at the Henry M. Jackson Foundation, Rockville, MD, and James Mullins and colleagues at the University of Washington, Seattle, WA.

SynchAligns—synchronize alignments

Purpose Align two different alignments of the same gene region or protein to each other. The two alignments need not cover the identical genomic span but they must overlap. One application of this tool is combining a reference or database alignment with a novel set of study sequences.

Background A SynchAligns option was initially added to the BioEdit sequence editor [BioEdit] at the suggestion of the HIV database. The HIV/HCV database version uses align0 [Myers & Miller, 1988] to align one sequence from each alignment; the gaps that were inserted into each sequence are then applied to the rest of the alignment, and the two alignments are concatenated.

Input options The user may specify a reference sequence common to both alignments to be used in synchronizing. Failing that, the program will select the longest sequences from each alignment to use as references. Gap characters and whether to squeeze them can be specified. The synchronized alignment can be trimmed to the region of overlap between the two component alignments.

Output A single synchronized alignment in the same format as the second input file or "pretty-printed" versions of this alignment.

Example:

```
align1  GSEEL-RSLY-NTVATL
        GSEELMRSLYMNTVATL
        GSEELMRSLY-NTVATL

align2  EELRS-LYNTVATLYCVHQ
        EELRSPLYNTVATLYCVHQ
        EELRSPLYNTVATLYCVHQ
        EELRSPLYNTVATLY-VHQ
```

Result after SynchAligns:

```
       GSEEL-RS-LY-NTVATL-----
       GSEELMRS-LYMNTVATL-----
       GSEELMRS-LY-NTVATL-----
       --EEL-RS-LY-NTVATLYCVHQ
       --EEL-RSPLY-NTVATLYCVHQ
       --EEL-RSPLY-NTVATLYCVHQ
       --EEL-RSPLY-NTVATLY-VHQ
```

History and context This tool was developed at our sister database, the Los Alamos HCV database, by Carla Kuiken and Charles Calef, and is included in the HIV database tools as well.

PrimAlign—explore DNA primer diversity

Purpose PrimAlign generates an alignment of your nucleotide sequence against our complete genome alignment.

Background PrimAlign can be used to rapidly assess variation in primers, functional domains, or any HIV nucleotide sequence of interest. The HIV complete genome alignments are meant to approximate a population survey. They are updated annually and include only a single sequence per person, but still have sampling biases.

If obtaining an alignment of all sequences in the database is desired, or just a subset (for example, all Ugandan D subtype sequences in the database that span the fragment) the Sequence Locator tool can be used to find the

Figure I-C.1: PrimAlign sample output

```
QUERY                ATGGGTGCGA GAGCGTCAAT ATTAA
A1.BY.97.97BL006     -YR------- --------G- -----
A1.KE.00.KER2008     .......---- --------G- -----
```

boundary positions of the fragment in the HXB2 genome, and these can be used to extract all sequences covering that region directly from the search interface of the HIV database [Gaschen *et al.*, 2001]. But beware, such database searches often can return hundreds of sequences from one subject if, for example, the individual was enrolled in a longitudinal study.

Input The direct sequence or its reverse complement (for primers) can be used as input.

Output A map that shows the position of the query relative to the HXB2 reference strain and an alignment of the fragment to all sequences from the same region in our curated alignment of complete genomes. Sequences whose names are printed in red are identical to the query. A simple fasta version of the alignment is available for downloading. Sequences include the subtype (A1 in the example below), followed by the country where the sample was taken (BY), the year of the sample (97), and finally the sequence name (7BL006).

History and context This tool was developed in parallel with its protein analog Epilign by Satish Pillai and Bette Korber, with support from Charles Calef. The alignment strategy and output options were later improved by Charles Calef and Brian Gaschen.

Epilign—explore epitope diversity

Purpose Epilign generates an alignment of your protein sequence against our web-based protein alignments.

Background Epilign can be used to get a rapid overview of the variability of an epitope, peptide, or protein. The location of the input sequence is automatically determined, and it is aligned to the HIV-1 database protein alignments, which excludes very similar sequences (e.g., multiple clones from one isolate, multiple sequences from one person), and so is meant to be a population survey.

Output A map (not reproduced here—see Figure I-C.5 in Sequence locator, below) is generated that shows the position of the query relative to the HXB2 reference strain. An alignment of the fragment to all sequences from the same region in our curated protein alignments is also created. Sequences whose names are printed in red, are identical to the query. If there are gaps in the main protein alignment, there is an option to squeeze the gaps and shift the sequence towards the C-terminal end. This is how potential T-cell epitopes would be seen by the immune system. The alignment is available for downloading in three simple formats. On the output page are two buttons that summarize the frequency of variants of your query. This analysis can be done for the entire alignment or for each subtype groups in the alignment.

Figure I-C.2: Epilign sample output, alignment results

```
       Query         SLYNTVATL
A1.KE.86.ML170       --F------
A1.KE.94.Q23         --F------
A1.SE.94.SE7253      --F----V-
A1.SE.94.SE7535      ---------
A1.SE.95.SE8538      ---------
```

Figure I-C.2 shows the top of the alignment for the SLYNTVATL epitope. The sequence names indicate the subtype (A1), the two letter country code (KE for Kenya), year of sampling (86 for 1986) and the sequence name.

Figure I-C.3: Epilign sample output, summary by subtype

```
Variant          Count    Percent
SLYNTVATL
---------        7        53.8
--F------        3        23.1
--F----V-        2        15.4
-------V-        1        7.7

   Total sequences = 13
Number of variants = 4
```

Figure I-C.4: Epilign sample output, subtype histogram

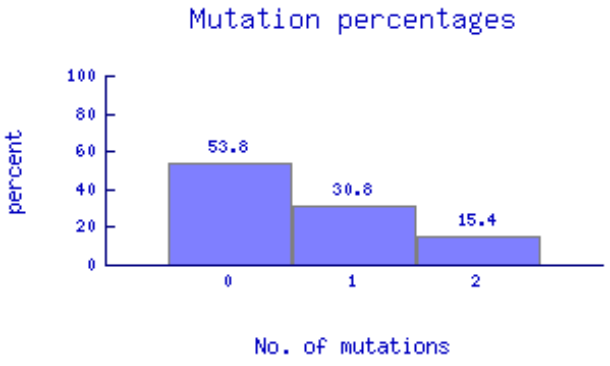


Figure I-C.3 summarizes the variation of the A1 subtype for this epitope. Of 13 A1 subtype sequences, 53.8%

are identical, and 23.1% differ from the query by having only an F substitution at position 3. These data are also presented in histogram form (Figure I-C.4). Further summaries of each kind of variant in every subtype are also provided but not shown here.

History and context This tool was developed in parallel with its nucleotide analog, Epilign, by Satish Pillai and Bette Korber, with support from Charles Calef. The alignment strategy and output was improved by Charles Calef and Brian Gaschen. Richard Koup (NIH) suggested adding the graphical representation of the identities in each subtype.

Sequence locator—HIV/SIV sequence locator tool

Purpose Finds the genomic position of a nucleotide or protein sequence in HIV-1/SIVcpz or HIV-2/SIVsmm/SIVmac relative to the reference strains HXB2 and SMM239.

Background Because HIV sequences vary in length, inconsistent and inaccurate numbering of locations in HIV DNA and protein sequences remains a problem in the literature. Positions published without reference to a strain (for example Gag positions 242–251), are meaningless because insertions and deletions change the length of HIV proteins. Often the numbers are not precise and do not match the reported sequence. This tool enables publication of precise and accurate positions relative to our reference strain HXB2 (GenBank accession number K03455). See the HIV database reviews about HIV and SIV numbering for more details [Korber *et al.*, 1999; Calef *et al.*, 2002a].

Output The query HIV epitope SLYNTVAAL produces the output shown in Figure I-C.5.

The "NA position relative to the HXB2 genome start" can be used as input on our sequence search interface to retrieve sequences of interest that span a given region. A user can also input HXB2 positions (e.g., p17 77–85) and retrieve the corresponding amino acids.

History and context This tool was initially designed and implemented by Bette Korber and Satish Pillai, with input from Joseph Sodroski at Harvard. Improved versions of this code were designed and developed by Charles Calef with input and the addition of the SIV locator from Brian Foley, John Mokili, Bette Korber, and Carla Kuiken.

HIV BLAST

Purpose Performs a BLAST search [Altschul *et al.*, 1997] restricted to the HIV Sequence Database.

Background The interface can handle both nucleotide and amino acid sequences, and calls these searches either BLAST or TBLASTN, respectively. In addition, you can access a smaller BLAST database that excludes sequences whose subtype is unknown; this restricted database can help identify the likely subtype of the query. HIV-1 specific BLAST results can be particularly useful for identifying potential contamination events. If the query perfectly matches a common lab strain, contamination may be indicated. While traditional BLAST searches explore vast databases looking for statistical support of genetic relationships, virtually all HIV and SIV sequences are statistically highly related. BLAST searches are useful simply to identify the closest sequences in the current database.

Output Aside from the standard BLAST scores and query/match alignments, you can also download all or a selection of the sequences your BLAST search finds. If you choose the 'master-slave' output option, the downloaded sequences will be aligned. If you choose 'pairwise', the downloaded sequences will not necessarily be aligned. Output includes the sequence name, sampling country, and subtype, which are not provided by an NCBI search.

History and context This derivative application of the search tool developed at NCBI was suggested by Carla Kuiken and Bette Korber, and implemented by Charles Calef.

SUDI—Determining if a new subtype or sub-subtype has been identified

Purpose Helps determine if a newly defined clade of related sequences should most appropriately be considered a new subtype, a new sub-subtype, or part of a previously defined subtype.

Background SUDI was created at the request of participants in the 2000 HIV nomenclature committee [Robertson *et al.*, 2000a,b]. SUDI's purpose is to determine tree-based genetic distances for a new cluster relative to known subtypes, and then to compare these distances to typical distances found among pre-existing subtypes. Because absolute levels of similarity will depend on the region under consideration, the time of sampling in an ever-diverging epidemic, and the specific alignment, no absolute criteria for intra- and inter-subtype distances are included.

Input SUDI can use either an alignment or the outfile of a PHYLIP tree building program. The default tree for the program is a PHYLIP neighbor-joining tree built using an F84 model. If users want to base the analysis on a different tree, then a user tree can be created with PHYLIP, and the PHYLIP outfile can be used as the input for SUDI.

Figure I-C.5: Sequence locator sample output

Organism: **HIV**

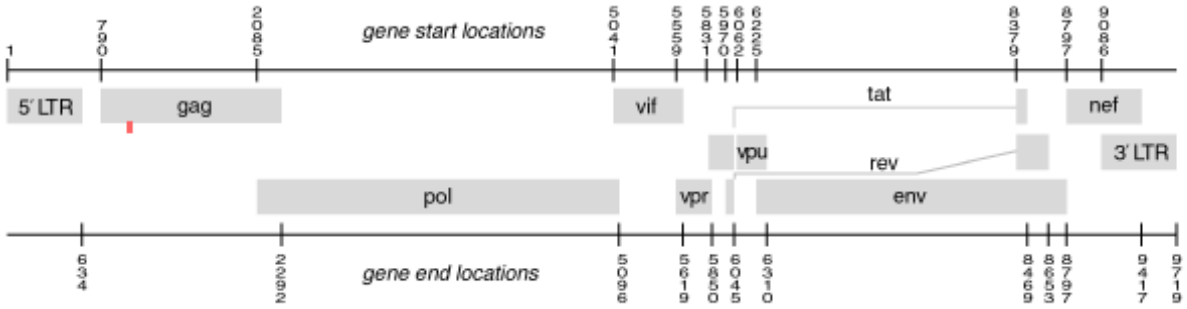


Table of protein regions touched by query sequence. AA = amino acid, NA = nucleic acid.				
CDS	**AA** position relative to protein start in HXB2	**AA** position relative to query sequence start	**NA** position relative to CDS start in HXB2	**NA** position relative to HXB2 genome start
Gag	77->85	1->9	229->255	1018->1044
p17	77->85	1->9	229->255	1018->1044

Alignment of the query sequence to HXB2:

```
Query SLYNTVAAL  9
      :::::::.:
HXB2  SLYNTVATL
```

Alignment of the protein and nucleotide equivalents of the query region in HXB2:

```
HXB2 DNA TCATTATATAATACAGTAGCAACCCTC  1044
HXB2 PRO _S__L__Y__N__T__V__A__T__L_
```

Output Based on the tree, histograms will be generated showing the range of intra-subtype distances, inter-subtype distances, and sub-subtype distances. The category that a given pairwise distance is assigned to (intra-subtype, inter-subtype, or sub-subtype distances) will depend on how the sequence was labeled (A_, B_, . . .) and how the clusters were defined. The cluster of sequences that the user is interested in, those sequences labeled 'U', will be highlighted. The U intra-subtype distances will be shown, and the U inter-subtype distance relative to the subtype closest to U will be shown. This way the user can determine if the novel cluster should be broken into sub-subtypes, or be considered part of a previously defined subtype.

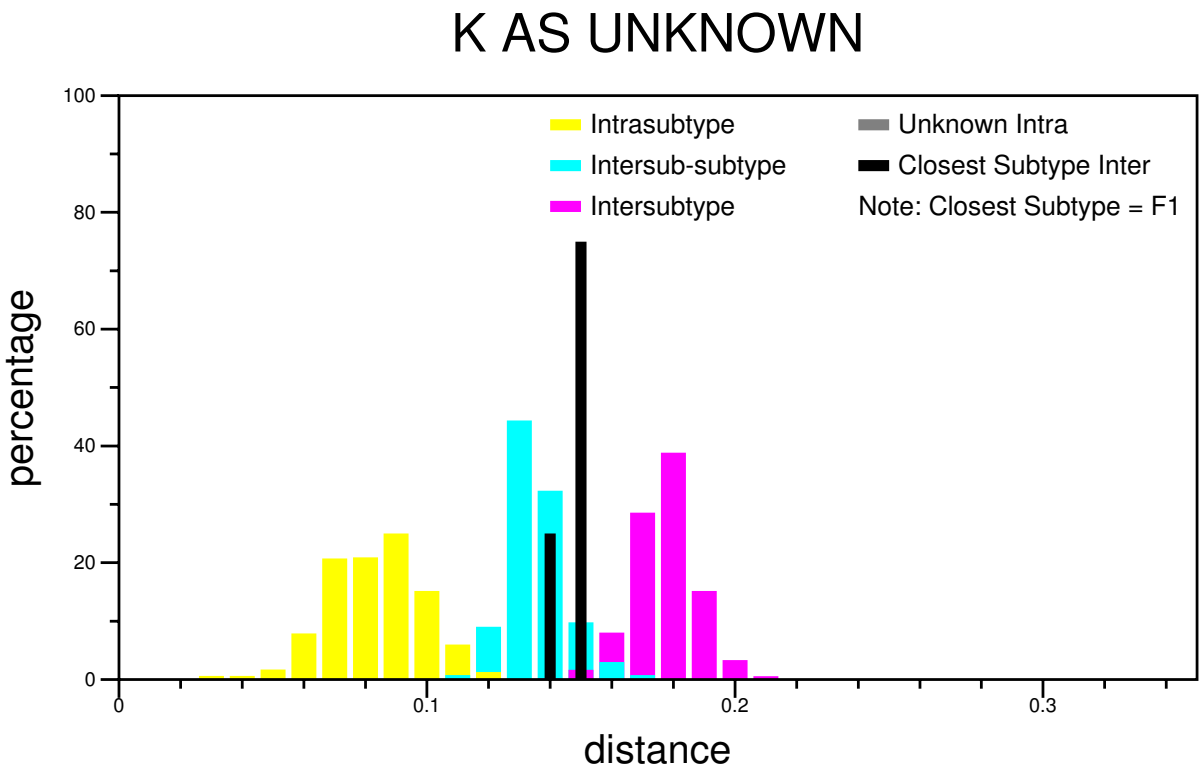
History and context SUDI was written by Bette Korber and Bob Funkhouser. Patrick Rose assisted with the interactive web interface.

RIP

Purpose The Recombinant Identification Program (RIP) is a computer program developed at the HIV Database to identify genetic sequences that appear to be mosaics of members of distinct phylogenetic clades. The idea is that such mosaic sequences are likely recombinants [Siepel *et al.*, 1995].

Background RIP was designed to detect recombinants of sequences belonging to different subtypes of HIV-1, but it can be used for other applications, including analysis of non-HIV sequences. The program moves a "window" of specified length stepwise across an alignment containing a query sequence and several background representatives. For each step in the window's progression across the genome, the query is compared to each of the background representatives within the window, and similarity is quantified as the fraction of identical base pairs. The values are

Figure I-C.6: SUDI sample output



retained, and the window is advanced one position. After the window has traversed the alignment from left to right, the program displays output revealing which background representative the query sequence most resembles at all possible positions. So-called "best matches" are marked if they are significant according to a statistical test.

Input There are three options for creating the alignment that RIP analyzes. 1. You may submit a single sequence, the query, and have RIP align it automatically to the subtype consensus alignment. 2. You may submit a single sequence, the query, and then build a custom background of sequences by selecting from a list provided on the website. 3. You may submit an alignment of your own that you have built with your query as the first sequence in the alignment. This option runs faster than the other two because RIP skips the alignment step. The size of the sliding window and the statistical significance threshold can be adjusted by the user. Gaps in the alignment can be handled in four different ways.

Output The default output consists of graphs showing the distances between the query sequence and the background set for each window position, and an alignment annotated with the best match sequence and whether or not it is statistically significant.

History and context A sliding window approach to identifying recombination events was first developed by Bette Korber and Adam Siepel [Siepel *et al.*, 1995]. In the fall of 1995 we used RIP to scan the HIV Database's env and gag master alignments for intersubtype recombinants [Siepel *et al.*, 1995]. Since its original development, RIP's web interface has been much improved by Thomas Leitner, Carla Kuiken, Brian Gaschen, Bette Korber, and Charles Calef.

Draw CRF—Make a figure to graphically represent recombinant genomes

Purpose Draws maps of HIV-1 genomes that are known to be recombinant. The different subtypes that comprise your genome appear as colored regions in the map.

Input The data used by the program record the points at which each component subtype in the genome begins and ends. If exact breakpoints are not known, there is a mechanism for entering uncertain boundaries. The breakpoint coordinates should be in standard HXB2 coordinates. The program can convert your data to HXB2 coordinates automatically if you select that option. A sample of input data looks like this:

```
1 2677 G
2678 3345 A
```

Figure I-C.7: RIP sample output

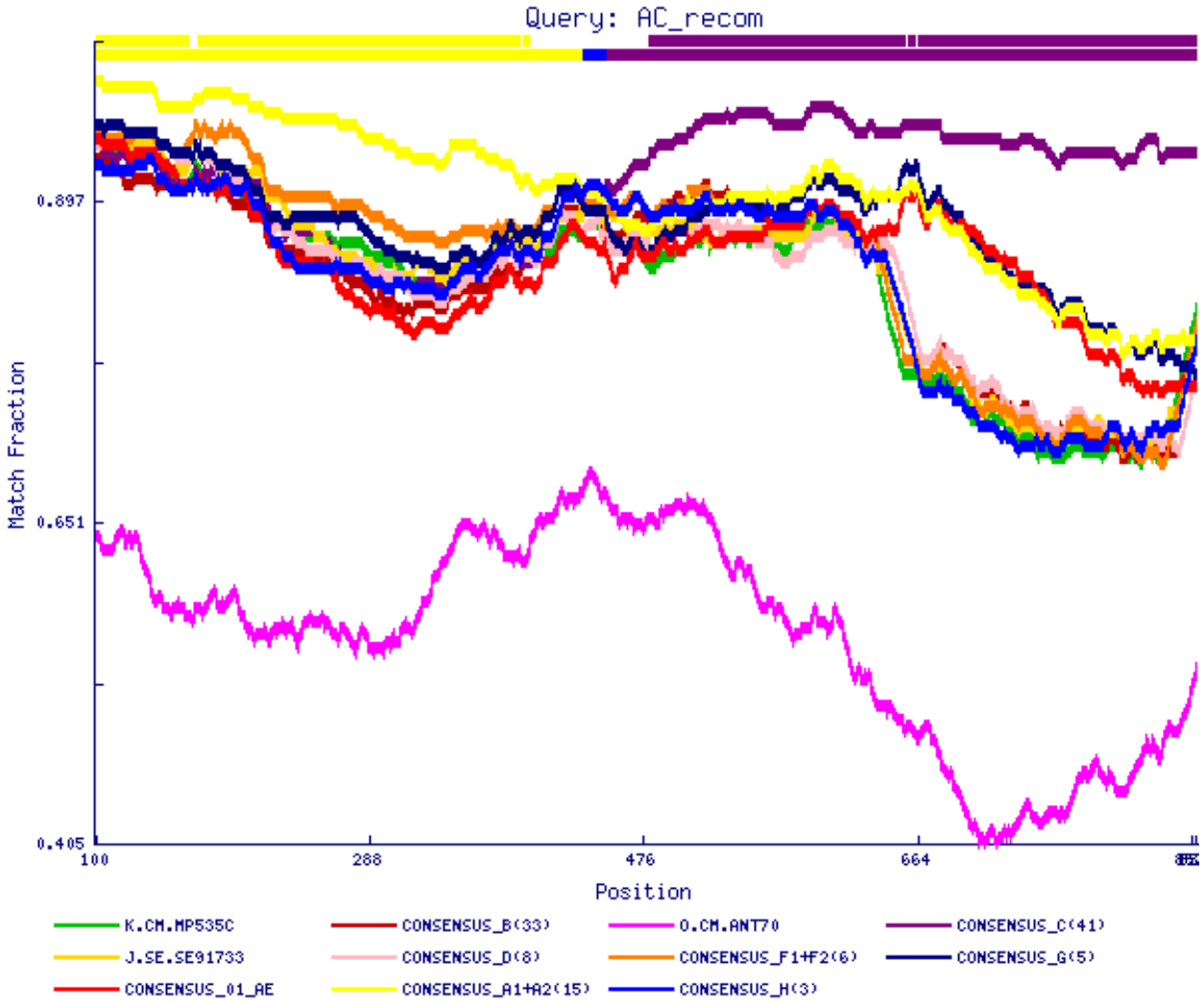
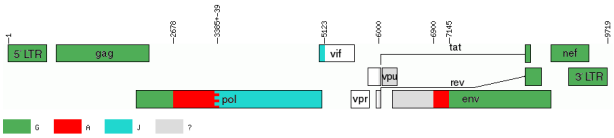


Figure I-C.8: RIP sample output

```
                                                
```

```
3346 3423 AJ
3424 5123 J
6000 6899 ?
6900 7144 A
7145 9719 G
```

Figure I-C.9: Map of mosaic HIV-1 genome whose breakpoint data is presented above.



Output The various subtype regions of the genome appear as different colors. Gray is used to illustrate regions of uncertain subtype. Uncertain breakpoint boundaries are illustrated on the map by an interfingering of the two colors that make up the two flanking regions; the breakpoint is shown at the center and expresses the size of the regions using a plus or minus notation. Regions with no data appear uncolored in the map.

History and context This tool was developed by Charles Calef with design suggestions from Thomas Leitner.

VESPA—Viral Epidemiology using Signature Pattern Analysis

Purpose Identifies sites which are common in one group of sequences, and are rare in another group.

Background VESPA detects signature patterns (atypical amino acid or nucleotide residues) in a set of query sequences relative to a set of reference sequences [Ou *et al.*, 1992; Korber & Myers, 1992]. It can be used to detect amino acids that characterize differences between two groups of sequences. It compares two groups of sequences and looks for a "signature" pattern, or the set of amino acids that is conserved among each set, but differing between the sets. VESPA will pick out those distinguishing amino acids, and calculate their frequencies in each set. Nucleotide alignments can also be used; however, amino acids are used as representative examples in the following discussion.

VESPA calculates the frequency of each amino acid (or nucleotide) at each position (column) in an alignment for the query and reference set, and selects the positions for which the most common character in the query set differs from that in the background set. The frequencies of characters at the distinguishing sites are also calculated [Ou *et al.*, 1992; Korber & Myers, 1992]. VESPA can also be used to compare the query and background sets' similarity in amino acid length, total charge, and amino acid content.

The sequences should all be of the same length, so if some sequences are shorter than others, the user should insert stars (∗) to complete the sequences, to indicate that no information was available at those sites. Positions with stars will be discounted from frequency calculations. Insertions made to maintain the alignment should be dashes (-); positions with dashes will be counted, and included in the signature pattern analysis.

The allowed characters for inclusion in an alignment are valid one-letter amino acid codes, -, and ∗; lower case letters are treated the same as uppercase letters. An asterisk is treated as 'missing', as will any other character; these will not be counted in the signature pattern tally. Therefore, if you have a stop codon and you label it as a dollar sign, it will be treated as if you have no information at that site.

The tool can also calculate various statistics, such as the amino acid frequencies in each group, the number of conserved signature amino acids in each sequence, and the amino acid content, amino acid length, and total charge.

History and context VESPA was originally written by by Bette Korber. Mark Flynn created the web interface and implemented a number of suggestions by Bette Korber and Carla Kuiken.

PCOORD—Principal Coordinate Analysis

Purpose PCOORD is a procedure to identify meaningful multivariate patterns in sequence data.

Background The Principal Coordinate Analysis method is very similar to regular Principal Component Analysis. The method was developed by the statistician J. C. Gower [1966]. PCOORD attempts to summarize the variation in the sequences in a limited number of axes or dimensions. A "dimension" is basically a combination of positions in a sequence that behave similarly, for example, "Position 133 usually has an A when position 250 has a G." One way to describe the process of finding these dimensions is as follows. If we have a two-dimensional swarm of datapoints, then we need two dimensions (the x and y axis) to describe the variation in our data. However, if the swarm is very elongated and the points almost lie on a straight line, then we really need only one dimension, although we use two. PCOORD uses a mathematical method to find the best way to describe a multi-dimensional dataset in a smaller number of dimensions, which are linear combinations of the original dimensions.

The dimensions are not necessarily biologically meaningful, but they can be. Quite frequently, some dimensions

that are extracted correspond to an epidemiological variable or some other feature of the data. The patterns that are found using PCOORD usually can be seen in a phylogenetic tree as well, but they may be much less pronounced there.

Output Each sequence gets a score on each of the dimensions, and these scores can be plotted pairwise. The coordinates can be downloaded, so that a better-looking graph can be produced with a spreadsheet or graphing program. The PCOORD program can identify each sequence with a character (number, letter, or symbol such as $*$ or ^). To use that feature, you need a file with one character for each sequence. In the dimension plot, the point representing each sequence will then be identified by the corresponding character.

History and context The PCOORD program suite was developed by Des Higgins [1992] (then at the EMBL), and adapted for the UNIX platform by Jack Leunissen of the CAOS/CAMM institute in Nijmegen, The Netherlands. The web interface was created by Kersti Rock based on specifications by Carla Kuiken [Kuiken *et al.*, 1993; Potts *et al.*, 1993; Kuiken *et al.*, 1994].

Hypermut

Purpose Hypermut highlights hypermutational changes among other base mutations [Rose & Korber, 2000]. It takes a nucleotide alignment and documents the nature and context of nucleotide substitutions in a sequence population relative to a reference sequence.

Background A retroviral provirus is considered hypermutated if it undergoes an inordinate number of identical transitions, usually guanine to adenine (G←A). Hypermutation most often results in the production of replication-incompetent virus. Several papers were published in 2003 describing a host cellular defense mechanism that induces hypermutation in reverse transcribed nascent retroviral DNA. The Vif protein of HIV seems to be able to counter this activity [Mangeat *et al.*, 2003; Zhang *et al.*, 2003; Lecossier *et al.*, 2003].

Identifying hypermutated sequences in a viral population can be critical when reconstructing viral phylogenies (to assess the effects of drug therapy, immune surveillance, etc.). The apparent rate of viral evolution can be dramatically exaggerated by hypermutated sequences, when in actuality these viruses are evolutionary dead ends; their profound divergence is an artifact of a single aberrant round of replication.

Input The first sequence in the input alignment will be used as the reference sequence for the entire analysis, so this sequence should be chosen carefully. For example, for an intrapatient set, the reference should probably represent the most common form in the first sampled time point. For a set of unrelated sequences, the consensus sequence for the appropriate subtype would be used. Also, you may choose to display a general or region-specific overview of your sequences.

Output Hypermut output consists of

- a data sheet summarizing the hypermutations,
- a graphical overview of all the sequences and their nucleotide changes,
- a graphical overview of all mutations in a selected sequence, and
- a table for allowing quick analysis of mutations resulting in stop codons.

The program allows either an overview of the complete sequence, or a detailed view of a subregion. The hypermutational changes are color coded.

History and context HYPERMUT was originally written by Bette Korber and web development was undertaken by Patrick Rose; improvements were made by Werner Abfalterer. Francine McCutchan, Jean Carr, and Feng Gao offered suggestions for additional analysis. An application of the method to the HIV database is described by Rose & Korber [2000].

N-Glycosite

Purpose This tool highlights and tallies potential N-linked glycosylation sites in an aligned set of protein sequences.

Background The N-linked glycosylation site pattern `N-x[ST]` (where `N` is asparagine, `x` can be any amino acid, and `[ST]` is serine or threonine) is called a sequon. N-Glycosite can be used for any protein alignment, but is particularly helpful for the HIV envelope as it is heavily glycosylated. Sequons vary in position and number, and glycosylation can be critical for protein function and for immune evasion [Zhang *et al.*, 2004]. The extent of actual glycosylation of a sequon depends on the context, which could be expanded to a four amino acid `Nx[ST]y` pattern where the amino acids in the `x` or `y` positions influence the glycosylation efficiency. In particular, proline in position `x` or `y` does not favor N-linked glycosylation. Thus we also provide `Nx[ST]` or `Nx[ST]y` summaries.

Input If you just want to tally the number of N-glycosylation sites, this can be done with unaligned sequences, but to track movement or changes in particular sequons, aligned sequences are necessary.

Output The initial output page contains links to all other output files. These include an alignment with the N-linked sites highlighted (Figure I-C.10), tallies of the number of sequons in every sequence in an alignment, figures showing the fraction of each position in an alignment that contains an asparagine (N) that is part of a sequon (Figure I-C.10), and tallies of the number of sequons in a window of user specified length moving through the protein alignment.

History and context Bette Korber developed a simple version of this code for analysis of acute infection sequences [Derdeyn *et al.*, 2004]. Ming Zhang then made a web interface and added many useful features suggested by Brian Gaschen and Bette Korber.

Entropy

Purpose Assigns a quantitative measure of diversity to every position in an alignment, and compares one alignment to another to see if there is statistically supported evidence for positions with increased diversity in one set relative to another.

Background This code provides one strategy for quantifying sequence diversity, using the information theory concept of Shannon entropy [Shannon, 1948]. This code was originally used to compare blood derived HIV envelope sequences from two data sets, and we found evidence for sites that were more variable in the blood than brain [Korber *et al.*, 1994]. A second application compared the variability of sequence positions to immunologically important regions. Here the Shannon entropy of each position was calculated, and compared to some other biological property that has been characterized for that position. For example, the number of distinct cytotoxic T-lymphocyte (CTL) epitopes that span a position inversely correlates with the variability of that position [Yusim *et al.*, 2002]. In this application, the entropy scores were compared with another score of biological interest, in our case CTL epitope density.

Output Entropy comes in two flavors, called Entropy-one and Entropy-two. To calculate the entropy for positions in a single alignment, use the Entropy-one interface. If you want to compare the entropy in two different sequence sets (they will need to be aligned to each other), use the Entropy-two interface.

Entropy-one also estimates the average entropy of all positions in a given window size, advancing the window by a user-specified length.

Entropy-two compares the entropy in to different sequence sets. To assess statistical significance, a user-specified number of Monte Carlo randomizations of two sequence sets can be performed, and a comparison of the difference in entropy between the real data and the randomized data sets can be used to determine whether a difference in entropy was likely to have been observed by chance alone or is significant.

History and context This code was originally written by Bette Korber [1994] with the Monte Carlo randomization implemented by James Theiler. Ming Zhang adapted it to the web and added features suggested by Brian Gaschen, Carla Kuiken, and Bette Korber.

SNAP

Purpose Calculates synonymous versus non-synonymous base substitutions for all pairwise comparisons of sequences in a codon-aligned nucleotide alignment.

Background SNAP is based on the method of Nei & Gojobori [1986]. You should be familiar with this paper before using this program.

Output The number of synonymous and non-synonymous codon changes are counted, as well as the number of potential synonymous and non-synonymous changes when comparing two sequences. Ambiguous codons or codons with insertions are excluded from the tally of compared codons. The output provides overall sequence distances as well as a codon by codon summary. One must be wary when doing typical statistical analysis of these values. Distributions of values that are far from Gaussian are commonly found, so you should either check to see if you have a Gaussian distribution, or default to the use of non-parametric statistics, like a Wilcoxon rank sum test. Therefore the averages given at the bottom are only meant as a crude guide. Also, if one uses the full column of values for all pairwise comparisons (say all values of dn for one set, compared to all values for another set) there is a non-independence of points issue to be considered. An alternative is the use of a sequence like a consensus or a best estimate of an ancestral sequence as the first sequence in the alignment, and then just use the comparison of the first sequence to all others rather than all pairwise comparisons.

History and context SNAP was written by Bette Korber [2001], and adapted for the web by Satish Pillai. It was one of the earliest attempts to analyze synonymous versus nonsynonymous mutation rates in a way that was not averaged over entire genes; more sophisticated tree-based methods were later developed, although this method is simple in concept and also tracks insertions and deletions, and so still merits consideration. An application of

Figure I-C.10: Section of output from an HIV hypervariable region with N's that might be glycosylated highlighted in red.

```
                    110         120         130         140         150
D.UG.94.94UG1141    LNCTN--WVT DTT------- -N-TT----- ---------- G-MANCSFNI
01_AE.CF.90.90CF11 LHCTK--AKL NDT------- YNGTAKLND- -------TIG DEVRNCSFNV
02_AG.CM.97.97CM8  LDCHD--YNS TSH-NYSSIS NNMTEEM--- -------EMK GEIKNCSFNM
CPZ.CM.-.CAM3       MECRK--VTF NSTSN----- RNKTSTMTTN SPNEKX---D STVKNCTFNM
```

Figure I-C.11: The fraction of each position that is an N embedded in a potential N-linked glycosylation site in an alignment of 8 sequences.

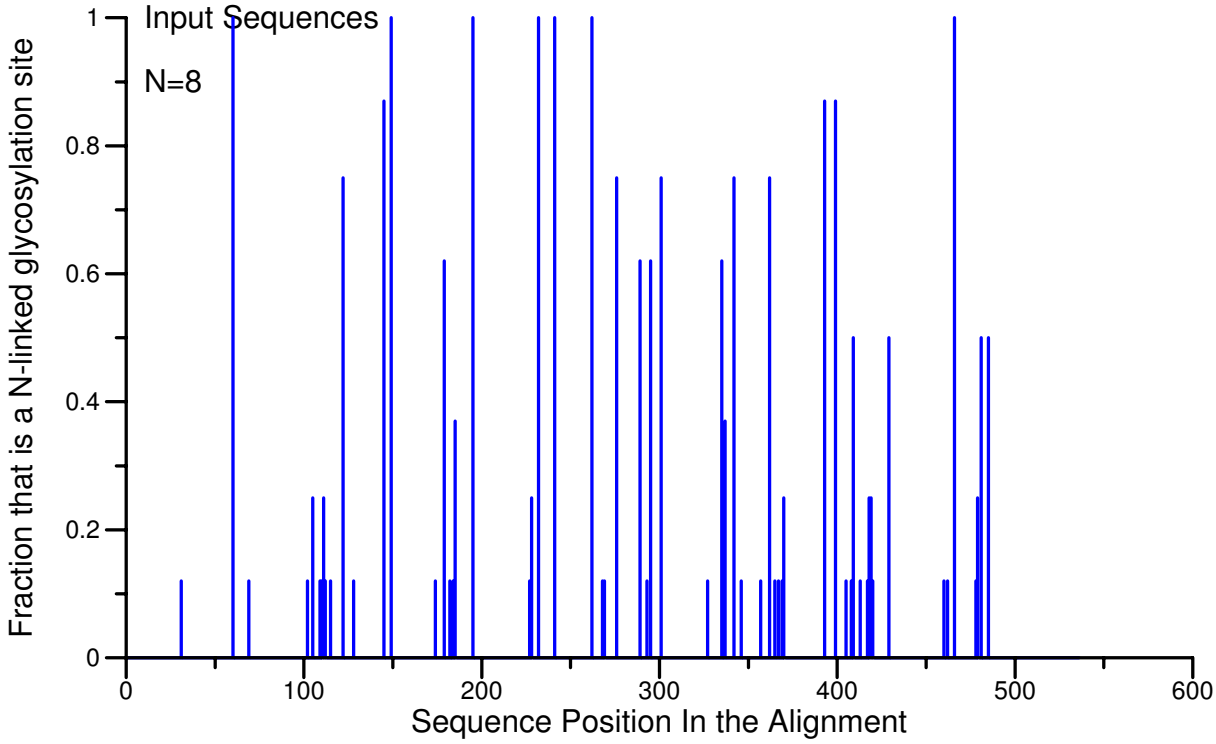
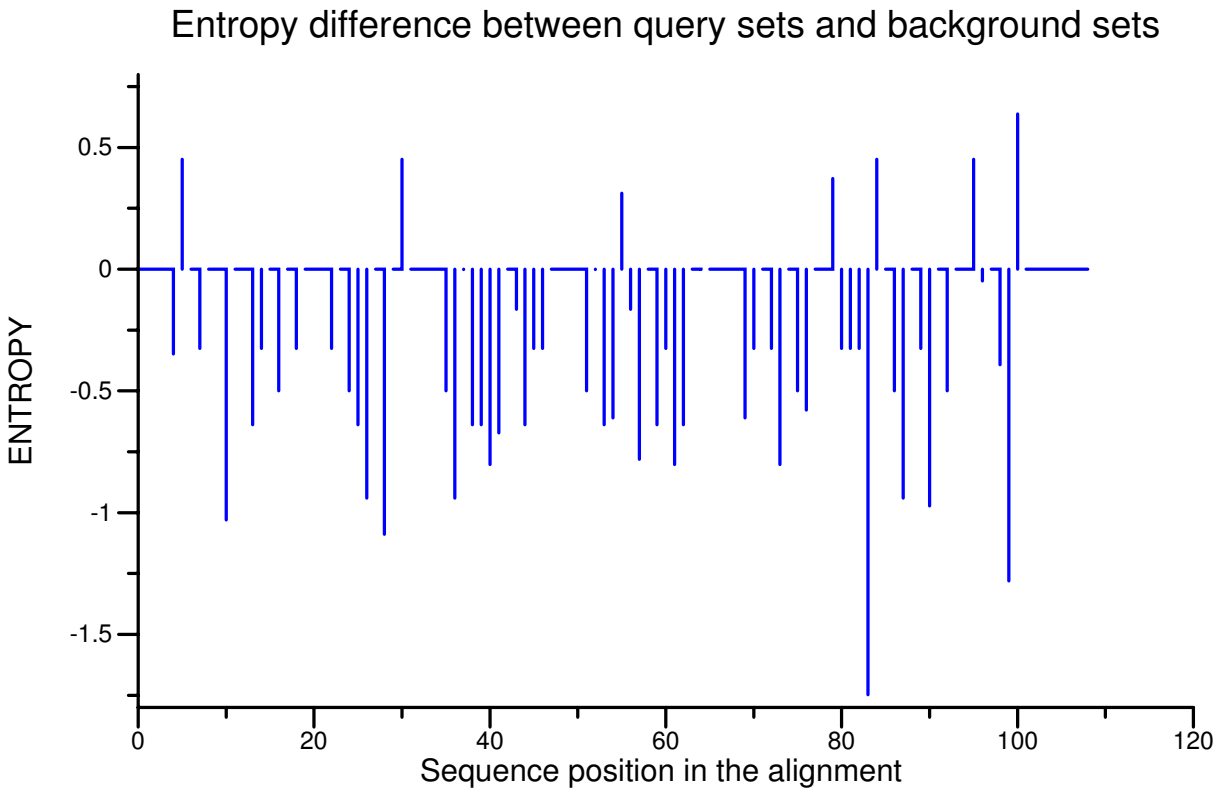


Figure I-C.12: The beginning of the output file that calculates the average entropy for each window of 15 with an overlap of 11. The Entropy tool can be used in conjunction with PeptGen tool to assign an average entropy score to each peptide as investigators are designing a panel of reagents. The top sequence is the consensus from the input.

```
         10         20         30         40
          |          |          |          |
LAEEEVVIRSENFTDNAKTIIVQLNESVEINCTRPNNNTRKSIHI
LAEEEVVIRSENFTD[Average entropy = 0.1778]
           NFTDNAKTIIVQLNE[Average entropy = 0.2795]
                      QLNESVEINCTRPNN[Average entropy = 0.3498]
```

Figure I-C.13: The difference in entropy between the two input files. The background file is more variable in positions that drop below the line, the query file in those that rise above the line.



the SNAP package is described in Ganeshan *et al.* [1997]. Statistical analysis was added at the suggestion of Yumi Yamaguchi-Kabata, following the method described in Ota & Nei [1994].

ADRA

Purpose Finds mutations associated with anti-HIV drug resistance in HIV-1 protease, RT, integrase, and envelope sequences. Accepts both nucleotide or amino acid sequence input.

Output Produces a table of resistance-associated mutations (Figure I-C.14) and an alignment with mutations indicated (Figure I-C.15). Tabulates drugs to which this sequence may show resistance and links to additional information on these mutations in the HIV Drug Resistance Database [Clark *et al.*, 2001].

History and context This tool was designed and written by Patrick Rose and Charles Calef as a way to explore the HIV Drug Resistance Database (`http://resdb.lanl.gov/Resist_DB/default.htm` maintained within our Los Alamos database by John Mellors.

TreeMaker

Purpose To produce "quick and dirty" trees. Our aim is not to make them dirty, but to make them quickly. These trees are generally not publication quality, but are meant to be used in an exploratory framework.

Background TreeMaker generates a neighbor-joining tree based on a sequence alignment. The tree is very basic and quite possibly not optimal for any dataset. The database tool FindModel, described below, can be used to determine the optimal model. We also provide a tutorial that gives some background information about phylogenetic tree construction, and provides further links.

Output The tree is displayed as a PNG file, and can also be downloaded as a PostScript or PDF file. Currently, the PHYLIP outfile and the Newick-formatted treefile can also be downloaded. By default, this interface uses the F84 distance model (also called "ML" because it is used in PHYLIP's maximum likelihood phylogeny program DNAML). This model incorporates different rates of transition and transversion, and also allows for different frequencies of the four nucleotides. Several other distance models are available. TreeMaker will be updated to use

Figure I-C.14: Table of mutations found in user's input that are known to confer resistance to HIV-1 antiretroviral drugs. The column on the right links to the full database record of this mutation.

• **Table of mutations potentially conferring resistance** (relative to HXB2r)

Protein	aa change	codon change	fold resist	cross resist	compound	record
Protease	L 10I	CTC/ATC	ND	ND	MK-639 (L-735,524, indinavir)	view
Protease	L 10I	CTC/ATC	ND	ND	Ro 31-8959 (saquinavir)	view
Protease	K 20R	AAG/AAA	ND	ND	ABT-538 (ritonavir)	view
Protease	K 20R	AAG/AAA	ND	Ro-31-8959 (8);	MK-639 (L-735,524, indinavir)	view
Protease	M 36I	ATG/ATA	ND	ND	ABT-538 (ritonavir)	view

Figure I-C.15: Alignment of user's nucleotide sequence, translated to protein and aligned to equivalent protein regions of HXB2. Mutations are indicated.

```
ALIGNMENT

P delineates the Protease gene region

QUERY NUC   CCTCAAATCACTCTT TGGCAACGACCCATC GTCACAATAAAAATA GGGGGGCAAGTAAGG GAAGCTCTATTAGAT
QUERY PRO    :  :  I  :  :   :  :  :  :  I   :  :  :  :  :   :  :  :  V  R   :  :  :  :  :
HXB2r PRO    P  Q  V  T  L   W  Q  R  P  L   V  T  I  K  I   G  G  Q  L  K   E  A  L  L  D   25
  MUTANTS          *                    *                                 *  *
            -P--P--P--P--P- -P--P--P--P--P- -P--P--P--P--P- -P--P--P--P--P- -P--P--P--P--P-

QUERY NUC   ACAGGAGCAGATGAT ACAGTATTAGAAGAT ATAAATTTACCAGGA AGATGGACACCAAAA ATGATAGGGGGAATT
QUERY PRO    :  :  :  :  :   :  :  :  :  D   I  N  :  :  :   :  :  T  :  :   :  :  :  :  :
HXB2r PRO    T  G  A  D  D   T  V  L  E  E   M  S  L  P  G   R  W  K  P  K   M  I  G  G  I   50
  MUTANTS                             *   *  *                 *
            -P--P--P--P--P- -P--P--P--P--P- -P--P--P--P--P- -P--P--P--P--P- -P--P--P--P--P-
```

the PAUP* based trees, similar to our tree building part of the search interface.

History and context This tool was originally developed by Carla Kuiken and Charles Calef. A completely new version of tree making is now part of our search interface (to be described in the 2006 compendium). This version is based on PAUP* and was made by Thomas Leitner, Charles Calef and Werner Abfalterer. We are grateful to Jim Wilgenbush who has given us permission to use PAUP* [Swofford, 2002] to infer our trees.

FindModel

Purpose FindModel analyzes your alignment to see which evolutionary model best describes the input sequences. This model can then be used to generate a better phylogenetic tree.

Background FindModel uses the program Weighbor [Bruno *et al.*, 2000] to generate the guide tree, based on Jukes-Cantor distances. Weighbor is used because it is much faster than maximum likelihood, but less biased and more robust than neighbor joining. Ziheng Yang's PAML [Yang, 1997] is used to calculate the likelihood. The AIC score, a version of the likelihood score that is weighted to compensate for the differences in degrees of freedom (or the number of parameters included) for each model, is calculated using the method described in Posada & Crandall [1998]. The standard log likelihood score is also reported, but the decision of the best fitting model is made based on the AIC. It is intuitively clear that a model that is more 'customizable' to the data, i.e., has more parameters, will usually produce a better fit. This would always result in the most complicated model being selected, even when simpler models would do almost as well. The AIC score compensates for this effect by weighting the likelihood

Table I-C.1: Partial view of the list of models and their AIC and likelihood scores.

Model name	AIC	LnL
JC : Jukes-Cantor (model 1)	3563.252246	-1781.626123
JC+G : Jukes-Cantor plus Gamma (model 3)	3504.693372	-1751.346686
F81 : Felsenstein 1981 (model 5)	3564.440496	-1779.220248
F81+G : Felsenstein 1981 plus Gamma (model 7)	3502.851558	-1747.425779
K80 : Kimura 2-parameter (model 9)	3499.844658	-1748.922329
K80+G : Kimura 2-parameter plus Gamma (model 11)	3423.016278	-1709.508139
HKY : Hasegawa-Kishino-Yano (model 13)	3499.375768	-1745.687884
HKY+G : Hasegawa-Kishino-Yano plus Gamma (model 15)	3412.457576	-1701.228788
TrN : Tamura-Nei (model 21)	3494.642212	-1742.321106
TrN+G : Tamura-Nei plus Gamma (model 23)	3413.187698	-1700.593849
GTR : General Time Reversible (model 53)	3487.768892	-1735.884446
GTR+G : General Time Reversible plus Gamma (model 55)	3411.658894	-1696.829447

score by the number of parameters for each model. FindModel, unlike Modeltest, does not allow invariant sites, because this feature is not implemented in PAML. This was a principled choice by PAML's author, because estimates of the fraction of invariant sites tend to be very sensitive to the number of taxa.

Finding the best evolutionary model is a computationally intensive procedure, both in its original implementation as the Modeltest PAUP* script and in our FindModel implementation. To reduce the computational burden on our servers, we have limited the default runs to a reduced set of models, and excluded those that do not have an obvious biological interpretation. The full set of models can be run, but has to be explicitly specified by checking the checkbox below the input section.

Output The output of FindModel consists of a list of models the program has tested, and their AIC and likelihood scores. The model with the smallest AIC score is shown as 'AIC-selected model'. This model is usually the best, and limited simulations have shown that FindModel shows very little tendency to over-fitting [Tao, in preparation]. In addition to the selected model, the FindModel output also shows a matrix (Figure I-C.16) that indicates which parameters are being estimated from the data in each model. By clicking on the model name, the matrix shows every parameter that is estimated separately in a different color. In Figure I-C.16, the Jukes-Cantor model shows that all transitions and transversions have the same color (orange) and therefore are represented by one parameter. The nucleotide frequencies are all shown as f_N, so they are also all estimated to be the same.

History and context FindModel was developed as a web implementation of the Modeltest script written by David Posada and Keith Crandall [Posada & Crandall, 1998], modified by Bill Bruno with input from Carla Kuiken.

PeptGen

Purpose PeptGen enables design of overlapping peptide sets from single proteins or alignments, with output that allows either visualizing the peptides and differences between them, or produces a list for ordering the peptides.

Background The algorithm to generate the peptides is complex and can be modified by the user in many different ways. For example, "forbidden" amino acids can be excluded from the ends of the peptide because of their inimical effect on binding to the HLA molecule. Peptides beginning with `Q` (glutamine) are thought to be unreliable, so `Q` has been made the default for N-term forbidden amino acids. The offset between one peptide and the next, i.e., the "width" of each stairstep, is determined by the "Overlap peptide by" parameter.

Output Figure I-C.17 shows the output for a protein fragment, where 15-mers overlapping by 11 were requested, but the amino acids `G`, `P`, `E`, `D`, `Q`, `N`, `T`, `S` and `C` were all disallowed at the C-terminal position.

When aligned sequences are provided as input, PeptGen creates an output that highlights the difference. This would be convenient for a situation where one wanted to design peptides to compare different subtypes, for example. To create the following peptides sets, no C-terminal amino acids were disallowed (so all peptides are length 15 except the last one, and two aligned sequences were given as input.

To generate a list of peptides ready to order, the set of peptides in Figure I-C.17 can be written out as a list with a unique ID assigned to each peptide, the peptide number, the sequence number, and a list of sequences

Figure I-C.16: Matrix showing free parameter estimation in the GTR (left) and Jukes-Cantor (right) evolutionary models.

General Time Reversible + γ

	T	C	A	G
T	f_T	a	b	c
C	a	f_C	d	e
A	b	d	f_A	f
G	c	e	f	f_G

Jukes-Cantor

	T	C	A	G
T	f_N	a	b	c
C	a	f_N	d	e
A	b	d	f_N	f
G	c	e	f	f_N

Figure I-C.17: Peptgen output for a single sequence. Disallowed C-terminal peptides are bold and underlined; not all peptides are 15 long to accommodate this. Their length is indicated in parentheses after the peptide.

```
MENRWQVMIVWQVDRMRIRTWKSLVKHHMYVSGKARGWFYRHHYESPHPRISSEVHIPL
MENRWQVMIVWQVDR (15) [-0.49]
    WQVMIVWQVDRMRIR (15) [-0.03]
        IVWQVDRMRIRTWK (14) [-0.54]
          WQVDRMRIRTWKSLV (15) [-0.61]
              RMRIRTWKSLVKHHM (15) [-0.92]
                  RTWKSLVKHHMYV (13) [-0.64]
```

that would contain the identical peptides from within the input alignment. One can request all peptides be listed, including duplicates between the two protein sequences, or that identical peptides be excluded so they don't need to be made twice.

History and context This site was designed by Charles Calef and Bette Korber [Calef *et al.*, 2001] in response to multiple requests by immunologists for help in generating peptides for epitope mapping. The request to facilitate peptide generation from alignments came from Richard Koup (NIH). Philip Goulder (Oxford) requested the ability to exclude certain amino acids from C-term positions, and Otto Yang at (UCLA) to forbid N-terminal amino acids. Andrew Bradbury (LANL) suggested calculating hydropathy for the resulting peptides, for antibody studies.

ELF—Epitope Location Finder

Purpose ELF scans a submitted protein sequence for known epitopes in our immunology database whose HLA agrees with the submitted HLAs.

Background ELF was written to identify potential epitopes within larger immunologically reactive target peptides [Calef *et al.*, 2002b]. Based on a peptide and a selection of HLA alleles, any known epitopes in that peptide are retrieved from in the immunology database, with links to the database entries and references. Those epitopes whose HLA presenting molecule agrees with the submitted HLAs are flagged. Anchor residues of potential epitopes that agree with the binding motifs of the submitted HLAs are indicated. Maps can be prepared that highlight every known epitope of the submitted HLA alleles across the HIV proteome. ELF can be used in conjunction with the Hepitope tool, which looks for enriched HLAs among people who make a reaction to the peptide in a population survey.

Output The output from ELF is very rich, so we have tried to make the page as uncluttered as possible. The first graphic on the output page is a map marking the location of the input peptide in the genome (see Figure I-C.5 in the sequence locator tool). Various links go to pages that contain:

- a list of the HLAs associated with your submitted HLA. As anchor motif information is spotty and this tool is exploratory, all related serotypes and genotypes will be incorporated in the search. For example, if the user were to enter either A2 or A*0202, all A2-related serotypes and genotypes with known anchor motifs would be examined.
- a list of all anchor motifs used in the search [Marsh *et al.*, 2000; Rammensee *et al.*, 1997, 1999]. Anchor motifs embedded in epitopes 8–11 amino acids long are considered, but larger epitopes would be missed.
- potential "epitopes" ordered by HLAs. This link takes you to a listing of possible epitopes in your peptide based on the presence of appropriately spaced anchor motifs.

A list of known CTL epitopes in the peptide (regardless of HLA type) can be useful for searching for unanticipated cross-presentation. The epitopes are linked to the corresponding records in the immunology database; these records provide information regarding escape mutations, clade specific reactions, immunodominance, etc., among epitope variants. Substitutions in the epitope relative to the query peptide are highlighted with red, and epitopes

presented by the requested HLAs are marked with a green arrow.

History and context This tool was first developed by Charles Calef, Rama Thakalapally, James Szinger, and Bette Korber [Calef *et al.*, 2002b] to attempt to define epitopes within reactive peptides to support experimental epitope mapping conducted at the University of Alabama by Richard Kaslow and Paul Goepfert [Bansal *et al.*, 2003]. Charles Calef has implemented improvements over time, incorporating new suggestions made by Carla Kuiken, Karina Yusim and Bette Korber, and Christian Brander at Harvard/MGH.

Motif Scan

Purpose Motif Scan is an HLA binding motif scanner that finds HLA anchor residue motifs within protein sequences for specified HLA serotypes, genotypes, or supertypes.

Background Two major motif libraries were used [Marsh *et al.*, 2000; Rammensee *et al.*, 1999] and the literature was surveyed for additional anchor motifs. The supermotifs incorporate anchor residues that are recognized by multiple alleles within the supertype [Sette & Sidney, 1999]. We store only anchor motifs in our libraries; to incorporate auxiliary amino acids you must input your own custom motif. The motif dictionaries we use are listed on the web, as is an abbreviated list of associations between HLA genotypes and serotypes.

Input The input for Motif Scan is obtained in two steps. The first step determines what anchor motifs are of interest. If you are interested in a functional motif or auxiliary and anchor motifs, you can input that instead, using the syntax `x[LM]xxx[K]xx[V]` where `x` allows any amino acid and determines the spacing, and locations where more than one amino acid is allowed are indicated by brackets: `L` or `M` in the second position, `K` in the sixth. The second step selects the sequences to be scanned. Predefined HIV protein sequences can be used, or you can upload your own sequences. Sequences are stripped of gaps before processing.

Output All motifs with identical search patterns are grouped together. C-terminal anchor amino acids are shown in magenta and anchor amino acids in the other positions are shown in cyan. If a given amino acid is matched by more than one motif, then it is highlighted as a C-terminal anchor amino acid. All anchor amino acids are shown in uppercase and non-anchors are lowercase. Following the sequences is a list of potential epitopes showing their positions in the input sequences. You can also view and download the resulting sequences in fasta format where the anchor amino acids are presented in uppercase and all the remaining ones in lowercase. The potential epitopes can be also downloaded in CSV (comma-separated value) format, which can be read into a spreadsheet.

History and context This tool was first developed by Warren Kibbe, Rama Thakallapally and Bette Korber [Thakallapally *et al.*, 2001]. Since the initial publication, the tool and the motif libraries were much improved by Karina Yusim and James Szinger [Yusim *et al.*, 2004].

Hepitope

Purpose Hepitope tests for HLA alleles that are enriched in individuals that react with a set of peptides.

Background This tool can be used in the context of a population study where HLAs and Elispot reactivity are available for a set of patients. To find HLA types that may be more frequent with certain reactivity patterns, a Fisher's exact test is used to look for enriched HLAs with a two-by-two contingency table tally for each subject tallying whether each HLA is present or absent, and whether they reacted to the peptide or not. This can be used in conjunction with our ELF program, which will scan a peptide for known epitopes in the database and for anchor motifs for HLAs that are found to be enriched, thus helping to identify epitopes within a larger peptide fragment (Hopeful Epitopes, or Hepitopes). This tool is not HIV or HCV specific, except when it is used in conjunction with ELF. The output is organized by peptide, and these can be returned either in the order entered or in alphabetical order. You can have all of the data returned, including summaries of every person's HLA that did not react with the peptide in question, but the default is to display only positive reactions.

Input This tool requires two inputs. The first input (Figure I-C.22) is a text format table of patients and their HLAs (note that many patients are needed to get statistical significance). The allele can be written as a serotype (A2) or a genotype (A*0201), but if both are used then they will be treated separately in the analysis. If an HLA type is unknown, it should be written as a single character. For example, if the C alleles had not yet been determined in Patient 1, then the HLA could be written as:

```
Patient1  A*0201 A*0201 B*5703 B*1701 C C
```

The second input is a list of reactive peptides, and the patients that reacted:

```
Gag1 MGARASVLSGGELDRWEK Patient1
Gag2 SGGELDRWEKIRLRPGGK Patient2 Patient3
Gag3 EKIRLRPGGKKKYKLKHI Patient4
```

Figure I-C.18: Known epitopes that are found within PQITLWQRPLVTIKIGGQ, the query peptide. Clicking on the aligned peptides links you to all of the database entries for the combination of peptide and the HLA presenting molecule. Clicking on the align button takes you to an alignment of this epitope extracted from the main database alignment. The green arrow denotes an epitope from the defined HLA set.

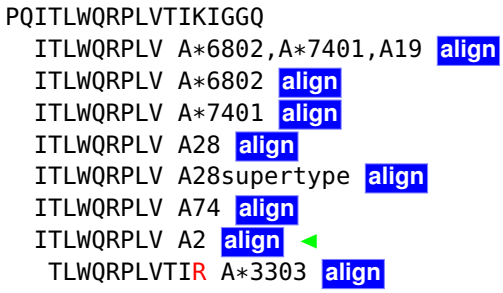
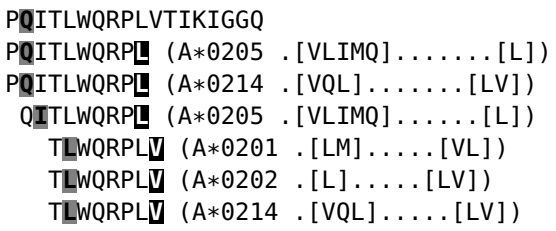


Figure I-C.19: Highlighting anchor motifs in the epitope. Identification of potential epitopes within the reactive peptide based on the anchor residues described for any HLAs related to the HLA of interest. C terminal anchors are marked in magenta, second position anchors in blue. No B44-related motifs were found.



Output Four columns of data that form the 2 by 2 contingency table used to compute the p-value. The output is arranged by peptide, and if the ELF integration is requested, anchor motifs and known epitopes are also summarized for each epitope.

a The number of individuals that carry the HLA allele and react with the peptide.

b The number of individuals that carry the HLA allele and do not react with the peptide.

c The number of individuals that do not carry the HLA allele and react with the peptide.

d The number of individuals that do not carry the HLA allele and do not react with the peptide.

The one-sided Fisher's exact test p-value is calculated to see if category *a* (number of individuals that both carry the HLA allele and react with the peptide) is higher than one would expect by chance alone. These are uncorrected p-values, and obviously multiple tests are being done, so these values should be evaluated with appropriate corrections or else the enriched HLAs for a give peptide should be considered as a hypothesis forming guideline for a suggestion of a likely HLA presenting molecule.

History and context This web-based tool and strategy for enabling epitope prediction analysis was developed by James Szinger and Bette Korber for a large epitope mapping and HLA typing project run by Christian Brander and Bruce Walker (Harvard University and Massachusetts General Hospital) [Kiepiela *et al.*, 2004].

I-C-4 Acknowledgements

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Figure I-C.20: Map of epitopes within the protease protein, in which this peptide was embedded. All known epitopes are indicated, with A2 and B44 known epitopes highlighted. More information regarding these epitopes could be obtained through the search page.

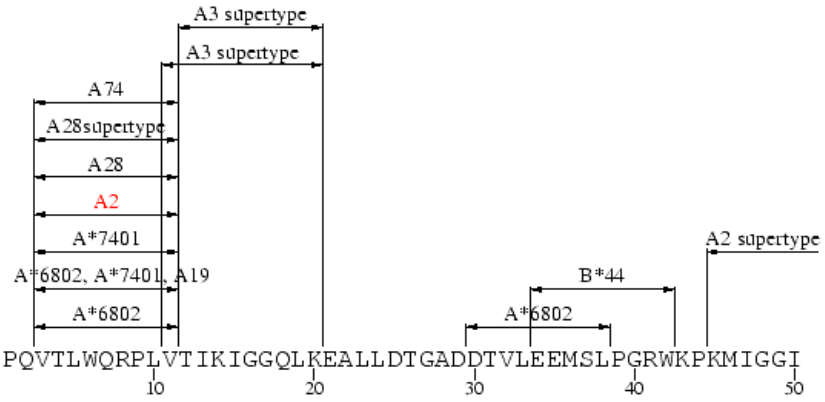

Figure I-C.21: Results of searching HXB2 Tat for HLA*0205 motifs that could give rise to epitopes of length 8, 9 or 10. The motifs that were scanned are listed first, in this case with spacing to give rise to 8, 9 or 10 amino acid long potential epitopes. A*0205 anchor residues are highlighted and capitalized in the Tat sequence, and the same possible epitopes are listed with their position number and spacing following the sequences.

```
>HXB2 x-[LQV]-x-x-x-x-x-[L] x-[LQV]-x-x-x-x-x-x-[L] x-[LQV]-x-x-x-x-x-x-x-[L] A*0205
mepvdprlep wkhpgsqpkt actncyckkc cfhcQVcfit kaLgisygrk   50
krrqrrrahq nsQthqasLs kqptsqprgd ptgpkekkkv eretetdpfd  100

Protein Position Sequence   Anchors
HXB2    62-69    SQTHQASL   .Q.....L
HXB2    35-43    QVCFITKAL  .V......L
HXB2    34-43    CQVCFITKAL .Q.......L
```

Figure I-C.22: Hepitope patient HLA sample input.

```
Patient1  A*0201 A*0201 B*5703 B*1701 Cw*0701 Cw*0705
Patient2  A*0201 A*0701 B*1202 B*0801 Cw*0701 Cw*0401
Patient3  A*1101 A*2403 B*0801 B*5801 Cw*0701 Cw*1501
Patient4  A*3002 A*3002 B*5802 B*5802 Cw*0602 Cw*0602
```

Figure I-C.23: Example of Hepitope output using a representative peptide. All HLAs found in reactive patients that recognize the peptide are listed. The full HLA type of the patients that react with the peptide is also listed. If the integration with ELF is selected, under each peptide will be a summary of known epitopes, links to references, and potential anchor motifs for the HLAs of interest within the epitope.

Peptide	Sequence	HLA Type	a	b	c	d	P
		B*1701	1	0	0	3	0.25000000
		B*5703	1	0	0	3	0.25000000
		Cw*0705	1	0	0	3	0.25000000
Gag1	MGARASVLSGGELDRWEK	A*0201	1	0	1	2	0.50000000
		Cw*0701	1	0	2	1	0.75000000

Patient	HLA
Patient1	A*0201 A*0201 B*1701 B*5703 Cw*0701 Cw*0705

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Part II

HIV CTL CD8+ Epitopes

II-A

Summary

This part includes tables, maps, and associated references of HIV-specific CTL epitopes arranged sequentially according to the location of the proteins in the HIV-1 genome. We attempted to make this part as comprehensive as possible, requiring that the epitope be contained within a defined region of a maximum of 30 amino acids, but not that the optimal boundaries be defined. Studies that were based on the analysis of whole proteins are described at the end of each protein section. The same epitope can have multiple entries, as each entry represents a single publication in this part of the database. For more recent updates, epitope sequence alignments, and useful search capabilities, please see our web site: `http://www.hiv.lanl.gov/content/immunology`. For a concise listing of the best defined CTL epitopes, see the summary by Nicole Frahm, Christian Brander and Philip Goulder on page 3 in Part I of this compendium. CTL responses to proteins with no defined epitopes are listed at the end of each protein section.

Recent studies utilize multiple functions attributed to T cells to define responses, and the simple distinctions of cytotoxic T-cell and helper T-cells have become blurred as more is learned about the range of responses triggered in CD4 and CD8 positive T-cells responding to antigenic stimulus. When adding the most recent studies to the database, we have tried to place T cell responses in a reasonable manner into our traditional helper T cell and CTL parts, and to specify the assay used to measure the response in each study.

II-A-1 Epitope tables

Each CTL reference has a multi-part basic entry:

HXB2 location: The viral strain HXB2 (GenBank Accession Number K03455) is used as a reference strain throughout this publication. The position of the defined epitope location relative to the sequence of the HXB2 protein is indicated. The numbering in this table corresponds to the protein maps. Because of HIV-1 variation the epitope may not actually be present in HXB2; rather, the position in HXB2 indicates the position aligned to the epitope. HXB2 was selected as the reference strain because so many studies use HXB2, and because crystal structures for HXB2-related proteins are often available. The precise positions of an epitope on the HXB2 reference strain can be readily obtained using the interactive position locator at our web site: `http://www.hiv.lanl.gov/content/hiv-db/LOCATE/locate.html`.

Author location: The amino acid positions of the epitope boundaries and the reference sequence are listed as given in the primary publication. Frequently, these positions as published are imprecise, and do not truly correspond to the numbering of the sequence, but they provide a reasonable guide to the peptide's approximate location in the protein. Also, in many cases the reference sequence identification was not provided, and in such cases it is not possible to use these numbers to specify precise locations.

Epitope: The amino acid sequence of the epitope of interest as defined in the reference, based on the reference strain used in the study defining the epitope. On occasions when only the position numbers and not the actual peptide sequence were specified in the original publication, we tried to fill in the peptide sequence based on the position numbers and reference strain. If the sequences were numbered inaccurately by the primary authors, or if we made a mistake in this process, we may have misrepresented the binding site's amino acid sequence. Because of this uncertainty, epitopes that were not explicitly written in the primary publication, that we determined by looking up the reference strain and the numbered location, are followed by a question mark in the table.

Epitope name: If the epitope has a name attributed by the publication, it is recorded here, e.g. "SL9".

Subtype: The subtype under study, generally not specified for B subtype.

Immunogen: The antigenic stimulus of the CTL response. Often this is an HIV-1 infection. If a vaccine was used as the original antigenic stimulation, not a natural infection, this is noted separately, and additional information about the vaccine antigen is provided as available.

Species (MHC): The species responding and MHC or HLA specificity of the epitope.

Donor MHC: The HLA genotype of the individual that responded to the epitope.

Country: The country where the samples were obtained—generally not specified if the study was conducted in the United States.

Assay type: Assay used to characterize the response.

Keywords: Keywords are a searchable field for the web interface that is included in the T-cell sections of the printed version to help identify entries of particular interest.

Reference: The primary reference (sometimes two or more directly related studies are included). Details for some of the earlier references are in Part V.

Following the entry for a given CTL epitope brief comments explain the context in which the epitope was studied and what was learned about the epitope in a given study.

II-A-2 HIV protein epitope maps

All HIV CTL epitopes mapped to within a region of 14 amino acids or less are indicated on the HIV protein epitope maps. The location and HLA restriction elements of CTL epitopes are indicated on protein sequences of HXB2. These maps are meant to provide the relative location of defined epitopes on a given protein, but the HXB2 sequence may not actually carry the epitope of interest, as it may vary relative to the sequence for which the epitope was defined. Epitopes with identical boundaries and HLA fields are included in the maps only once. If one laboratory determines HLA presenting molecules at the serotype level (example: A2) and another at the genotype level (example: A*0201) both will be included in the map. MHC specificities are indicative of the host species; when no MHC presenting molecule is defined, the host species is noted.

II-A-3 Alignments

To conserve space, no epitope alignments are provided in this book, but they can be generated using the CTL epitope search tool at `http://www.hiv.lanl.gov/content/immunology`. All epitopes are aligned to the HXB2 sequence, with the sequence used to define the epitope indicated directly above it. Sequences are sorted by their subtype and country of origin.

The master alignment files from which the epitope alignments were created are available at our web site[1]. The alignments were modified in some cases to optimize the alignment relative to the defined epitope and minimize insertions and deletions; epitope alignments are generated by anchoring on the C-terminal residue. A dash indicates identity to the consensus sequence, and a period indicates an insertion made to maintain the alignment. Stop codons are indicated with a `$`, and frameshifts by a `#`, or ambiguous codons (nucleotide was `r`, `y`, or `n`) by an `x`; they are inserted to maintain the alignments. In consensus sequences an upper case letter indicates the amino acid was present in all sequences, a lower case letter indicates the amino acid was present in most sequences in a given position, and a question mark indicates two or more amino acids were represented with equal frequency.

[1] `http://www.hiv.lanl.gov/content/hiv-db/ALIGN_CURRENT/ALIGN-INDEX.html`

II-B

HIV CTL Epitope Tables

All HIV CTL epitopes are arranged by protein position. The table entries are sorted in a nested way—first by protein, then by HXB2 start location and finally by HLA presenting molecule. CTL reactions against proteins with undefined epitopes are listed at the end of the protein that stimulated the response.

II-B-1 Gag p17 CTL, CD8+, epitopes

HXB2 Location p17 (5–13)
Author Location Gag (5–13 SUMA)
Epitope ASVLSGGEL
Epitope name Gag AL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T-cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location p17 (11–19)
Author Location
Epitope GELDRWEKI
Epitope name Gag-GI9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Donor MHC A*0201 A*0217 B*0801 B*4002 Cw*0303 Cw*070
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- This epitope was newly defined in this study.
- Patient 01RCH46 was Hispanic, on HAART, and had a viral load of 21000 and CD4 count of 623 – she also recognized KETINEEAA p24(70-78), HLA B*4002, and TAFTIPSI, RT(128-135), HLA A*0217.
- Among HIV+ individuals who carried HLA B40, 2/5 (40%) recognized this epitope.

HXB2 Location p17 (11–19)
Author Location p17 (11–19)
Epitope GELDRWEKI
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p17 (11–30)
Author Location Gag (11–30)
Epitope GELDRWEKIRLRPGGKKKYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B62)
Donor MHC A2, A32, B27, B62
Assay type Chromium-release assay
Keywords genital and mucosal immunity
References Musey *et al.* 2003

- CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments.
- CD8+ T cell clones directed at this epitope were derived from blood and semen.

HXB2 Location p17 (16–30)
Author Location p17 (16–30 HXB2)
Epitope WEKIRLRPGGKKKYK

Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p17 (18–26)
Author Location p17 (18–26 IIIB)
Epitope KIRLRPGGK
Immunogen
Species (MHC) human (A*0301)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes that this is an A*0301 epitope.

HXB2 Location p17 (18–26)
Author Location
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location p17 (18–26)
Author Location p17 (18–26 SF2)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
References Altfeld *et al.* 2001a

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- The reactive peptide p17 gag WEKIRLRPGGKKKYK contained two A*0301-restricted epitopes, KIRLRPGGK and RLRPGGKKK A*0301.

HXB2 Location p17 (18–26)
Author Location p17 (18–26)
Epitope KIRLRPGGK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8+ cells are found, each one constituting 30-40% of the CD8+ cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- Two of seven patients responded to this peptide with GzB producing cells, while none of the patients responded with IFN-gamma producing cells.

HXB2 Location p17 (18–26)
Author Location p17 (18–26 IIIB)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1996

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.
- KIRLRPGGR and RIRLRPGGR, naturally occurring variants, were found in mother and are escape mutants.

HXB2 Location p17 (18–26)
Author Location p17 (18–26)
Epitope KIRLRPGGK
Immunogen in vitro stimulation or selection
Species (MHC) human (A3)
Keywords dendritic cells
References Zarling *et al.* 1999

- This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses.
- Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA.
- A weak response to KLTPLCVSL was stimulated using macrophages as the APC.
- No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.

HXB2 Location p17 (18–26)
Author Location Gag (18–26)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Brodie *et al.* 1999

- The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptive transfer.
- The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively-infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects.

HXB2 Location p17 (18–26)
Author Location (18–26)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Brodie *et al.* 2000

- Study tracks and quantifies *in vivo* migration of neo-marked CD8+ HIV-specific CTL.
- Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication.
- The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism.
- This study provides a methodology for tracking and studying antigen specific CTL *in vivo*.

HXB2 Location p17 (18–26)
Author Location p17 (18–26 IIIB)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) transgenic mouse (A3)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- KIRLRPGGR and RIRLRPGGR were escape mutants.
- This epitope was recognized and many escape mutants were detected in an HLA A3 transmitting mother, and was recognized but invariant in an HLA A3 non-transmitting mother.

HXB2 Location p17 (18–26)
Author Location p17 (18–26 IIIB)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords review, escape
References Goulder *et al.* 1997e; Goulder *et al.* 1997a

- HLA-identical sibling hemophiliac brothers were both infected with the same batch of factor VIII. Goulder *et al.* [1997e] is a review of immune escape that summarizes this study.
- One had a response to this epitope, the other did not. They were tested 6-8 years after infection.

HXB2 Location p17 (18–26)
Author Location p17 (subtype B)
Epitope KIRLRPGGK
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A3)
References Kaul *et al.* 2000

- 11 of 16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8+ gamma-IFN responses in the cervix – systemic CD8+ T-cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T-cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T-cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location p17 (18–26)
Author Location p17 (SF2)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.

- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (18–26)
Author Location p17
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords HAART, ART
References Seth *et al.* 2001

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.

HXB2 Location p17 (18–26)
Author Location p17 (18–26 SF2)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 3/7 group 1, 0/4 group 2, and 2/2 group 3.

HXB2 Location p17 (18–26)
Author Location p17 (18–26)
Epitope KIRLRPGGK
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A3)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- KIRLRPGGK is cross-reactive for A, B, and D clades.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location p17 (18–26)
Author Location p17 (JRCSF)
Epitope KIRLRPGGK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Severino *et al.* 2000

- Primary HLA-A3+ CD4+ and HLA-mismatched lymphocytes from uninfected donors were infected with JRCSF after isolation then cocultured with the A3-restricted CTL clone 11504/A7 specific for KIRLRPGGK, and viral inhibition was MHC-restricted.
- Primary monocytes and monocyte-derived DC were generated from the same donors, replication of HIV-1 in these cell types was less efficient than in lymphocytes and could also be inhibited by MHC-restricted CTL.
- DC-lymphocyte cluster cultures allowed vigorous viral replication and MHC-restricted CTL viral inhibition was blunted or lost depending on the ratio of DC to CD4+ lymphocyte in the culture.

HXB2 Location p17 (18–26)
Author Location p17 (18–26)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP).
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.

HXB2 Location p17 (18–26)
Author Location p17
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords dendritic cells
References Ostrowski *et al.* 2000

- The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*.
- Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients.
- Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes.
- The T-helper epitope used for CD4+ T-cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)

HXB2 Location p17 (18–26)
Author Location p17 (18–26)

Epitope KIRLRPGGK
Epitope name A3-KK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), immunodominance, acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 8/14 HLA-A3 positive individuals had detectable A3-restricted responses during acute infection. Only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 7/8 individuals with acute responses had specific responses for this epitope.
- KIRLRPGGK and RLRPGGKKK were the most commonly recognized HLA-A3 epitopes during acute infection, after 1 year of treatment, and after STI. RLRPGGKKK was immunodominant.

HXB2 Location p17 (18–26)
Author Location p17 (18–26)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location p17 (18–26)
Author Location p17 (18–26 B consensus)
Epitope KIRLRPGGK
Epitope name KK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords epitope processing, immunodominance, escape, acute infection, characterizing CD8+ T cell responses, reversion, viral fitness
References Allen *et al.* 2004

- KK9 and RK9 overlap, are presented by HLA-A3, and are frequently immunodominant and involved in acute-phase primary responses. A mutation in the C-terminal flanking residue of KK9 (K to Q) (kirlrpkkg-Q) inhibits processing of the immunodominant gag KK9 epitope, resulting in rapid decline in the KK9 specific CD8+ T-cell response. At the same time it abrogates the response to RK9 through the embedded mutation rlrpggkQk. Transmission of this mutation to patients expressing HLA-A3 prevents acute-phase response to these epitopes, although the mutation can eventually revert to wild-type allowing a delayed response to the epitope.

HXB2 Location p17 (18–26)
Author Location p17
Epitope KIRLRPGGK
Epitope name KK9
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords review, epitope processing, escape
References Goulder & Watkins 2004

- This paper is a review of the role of CTL in HIV infection, and it uses KK9 as an example of an epitope that escapes due to a mutation beyond the epitope on the C-terminal side that probably affects proteasomal processing.

HXB2 Location p17 (18–26)
Author Location (B consensus)
Epitope KIRLRPGGK
Epitope name KK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, B14, B60, Cw3, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- One of nine individuals recognized this epitope.

HXB2 Location p17 (18–26)
Author Location p17
Epitope KIRLRPGGK
Immunogen HIV-1 exposed seronegative

Species (MHC) human (A3)
Donor MHC A01, A03, B39, B44, Cw4, Cw6
Assay type T-cell Elispot
Keywords HIV exposed persistently seronegative (HEPS)
References Missale *et al.* 2004

- HIV-specific T-cell response was tested in HIV-uninfected patients exposed to blood from a patient with highly replicating HIV; these same patients were nosocomially infected with HBV. HIV-specific T-cell responses were directed to structural and non-structural HIV proteins in two patients suggesting that the virus replicated in these patients sufficiently to prime a cell-mediated immune response that protected these individuals from HIV infection.
- This patient responded to 3/11 HIV epitopes tested in an IFNgamma EliSpot assay. Responses were detected 16 and 20 weeks after exposure, but were lost by week 80.

HXB2 Location p17 (18–26)
Author Location p17 (18–26)
Epitope KIRLRPGGK
Immunogen HIV-1 infection
Species (MHC) human (A3, A3.1, B27)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p17 (18–26)
Author Location p17 (18–26)
Epitope KIRLRPGGK
Epitope name A3-KK9 Gag
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords epitope processing, supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response. This epitope did not vary, although the response declined over time. The authors suggest this might be due to a downstream Arg -> Thr substitution at C+2 that may impair processing.

HXB2 Location p17 (18–27)
Author Location (C consensus)
Epitope KIRLRPGGKK
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p17 (18–27)
Author Location Gag
Epitope KIRLRPGGKK
Epitope name 1272
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A11)
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for KIRLRPGGKK: 36%. This epitope has been previously reported to be presented by A3, B27, B62, Bw62 and is an A11 binder, but was not confirmed as a CTL target in this study.

HXB2 Location p17 (18–27)
Author Location p17 (18–27)
Epitope KIRLRPGGKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong T-helper cell responses. Only patients starting with moderately high viral load (VL) were able to reduce the VL set point. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up.
- 8/14 patients recognized this epitope.

HXB2 Location p17 (18–27)
Author Location p17 (18–27 LAI)
Epitope KIRLRPGGKK

Subtype B
Immunogen
Species (MHC) human (B27)
References Brander & Walker 1996
- D. Lewinsohn, pers. comm.

HXB2 Location p17 (18–27)
Author Location p17 (18–27)
Epitope KIRLRPGGKK
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Birk *et al.* 1998b
- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (18–31)
Author Location p17 (18–31)
Epitope KIRLRPGGKKKYKL
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Birk *et al.* 1998b
- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (18–31)
Author Location p17 (18–31)
Epitope KIRLRPGGKKKYKL
Immunogen HIV-1 infection
Species (MHC) human (B62)
References Lubaki *et al.* 1997
- 82 HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of CTL response.
- A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response.
- A subject who was HLA-B62+ had CTL that recognized this peptide, and p24 LGLNKIVRMYS, and one additional unknown epitope.

HXB2 Location p17 (18–42)
Author Location p17 (18–42 IIIB)
Epitope KIRLRPGGKKKYKLKHIVWASRELE
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Jassoy *et al.* 1992
- Epitope recognized by CTL clone derived from CSF.

HXB2 Location p17 (18–42)
Author Location p17 (18–42 PV22)
Epitope KIRLRPGGKKKYKLKHIVWASRELE
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Jassoy *et al.* 1993
- HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.

HXB2 Location p17 (18–42)
Author Location p17 (18–42 BH10)
Epitope KIRLRPGGKKKYKLKHIVWASRELE
Immunogen HIV-1 infection
Species (MHC) human (Bw62)
References Johnson *et al.* 1991
- Gag CTL response was studied in three individuals.

HXB2 Location p17 (19–27)
Author Location p17 (19–27 JRCSF)
Epitope IRLRPGGKK
Subtype B
Immunogen HIV-1 infection
Species (MHC) scid-hu mouse (B*2705)
Keywords optimal epitope
References Frahm *et al.* 2004
- Noted by Brander to be B*2705.

HXB2 Location p17 (19–27)
Author Location p17 (19–27 LAI)
Epitope IRLRPGGKK
Subtype B
Immunogen
Species (MHC) human (B27)
References Brander & Walker 1996

HXB2 Location p17 (19–27)
Author Location p17 (19–27 JRCSF)
Epitope IRLRPGGKK
Subtype B
Immunogen HIV-1 infection
Species (MHC) scid-hu mouse (B27)
Keywords escape
References McKinney *et al.* 1999
- Epitope-specific CTL were infused in infected human PBL-SCID mice, and transient decreases in viral load were observed, however virus was not eradicated and the HIV-specific CTL rapidly disappeared.
- No escape mutants were observed.
- Control CTL were long lived in both infected and uninfected mice, showing the rapid loss of CTL was due to target interaction.

HXB2 Location p17 (19–27)
Author Location p17 (SF2)
Epitope IRLRPGGKK
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a
- WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 2/3 individuals that were B27+ had a dominant response to this epitope.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.

- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (19–27)
Author Location p17 (19–27)
Epitope IRLRPGGKK
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Day *et al.* 2001

HXB2 Location p17 (19–27)
Author Location p17 (19–27)
Epitope IRLRPGGKK
Epitope name IK9
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords immunodominance, escape
References Goulder *et al.* 2001b

- This B27 epitope is generally recognized only if there is escape in the B27 dominant epitope, p24 KRWIILGLNK.

HXB2 Location p17 (19–27)
Author Location Gag
Epitope IRLRPGGKK
Epitope name IK9
Immunogen HIV-1 infection
Species (MHC) human (B27)
Donor MHC A26, B27
Assay type CD8 T-cell Elispot - IFNγ
Keywords responses in children, rate of progression, immunodominance, escape
References Feeney *et al.* 2004

- Viral load in a perinatally infected child remained low until emergence of an escape variant (kTwiilglnk) in the immunodominant CTL epitope KRWIILGLNK when the child was 7.4 years old. The emergence of this escape mutation was followed by an increase in viremia and an increase in the number of targeted CTL epitopes, measured again when the child was 9.2 years old. A low level response to IK9 was the only other epitope recognized prior to the loss of immune control and broadening of the response, and was detected in the 7.4 year sample.

HXB2 Location p17 (19–28)
Author Location Gag
Epitope IRLRPGGKKK
Epitope name 1271
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A11, A3, B62, Bw62)
Donor MHC A03, A11, B14, B51, Cw08, Cw13
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for IRLRPGGKKK:43% Promiscuous epitope binding to A03, B62, Bw62 and A11.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- Three of the four individuals that responded to SLYNTVATL recognized HIV epitopes, and one individual who was A*0201, A31 and B51 and B58w4 recognized this epitope (previously described as HLA A3.1), as well as one other.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A*03)
Keywords review, escape
References Goulder *et al.* 1997e; Goulder *et al.* 1997a

- HLA-identical sibling hemophiliac brothers were both infected with the same batch of factor VIII.
- They were tested 6-8 years after infection. One had a response to gag A3 epitope RLRPGGKKK, the other non-responder carried the sequence RLRPGGKKC.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes that this is an A*0301.

HXB2 Location p17 (20–28)
Author Location p17
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location p17 (20–28)
Author Location p17 (20–28 SF2)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
References Altfeld *et al.* 2001a

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- The reactive peptide p17 gag WEKIRLRPGGKKKYK contained two A*0301-restricted epitopes, KIRLRPGGK and RLRPGGKKK A*0301.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Epitope name RK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Donor MHC A3, A11, B35, B51
Keywords mother-to-infant transmission
References Sabbaj *et al.* 2002a

- IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release.
- Tetramer analysis of breast milk and peripheral blood samples of one volunteer showed responses to RLRPGGKKK in both compartments, 0.65% of CD3+/CD8+ cells in breast milk, and 0.22% of CD3+/CD8+ cells in peripheral blood cells.
- The frequencies of responses in the two compartments differed, and 2/4 women who responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Goulder *et al.* 2000c

- Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten.
- A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Goulder *et al.* 1997f

- A control CTL line that reacts with this peptide was included in the study.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords inter-clade comparisons
References Cao *et al.* 1997a

- The consensus peptide of A, B, and D clade viruses is RLRPGGKKK.
- The consensus peptide of C clade viruses is RLRPGGKKH and is equally reactive.

HXB2 Location p17 (20–28)
Author Location p17 (SF2)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.

- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (20–28)
Author Location p17 (20–28 SF2)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 5/7 group 1, 2/4 group 2, and 2/2 group 3.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Epitope name RK9
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords acute infection
References Goulder *et al.* 2001b

- Responses to this dominant A3-restricted Gag epitope are present during the time of decreasing viral load in acute infection.
- Mutations in this epitope were observed in autologous clones of subjects who were A3-positive with a higher frequency than those who were A3-negative (P = 0.0002)
- These mutations are being sexually transmitted in adult infections.

HXB2 Location p17 (20–28)
Author Location
Epitope RLRPGGKKK
Epitope name Gag-RK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A03, 7/20 (35%) recognized this epitope.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Epitope name A3-RK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), immunodominance, acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06 was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 8/14 HLA-A3 positive individuals had detectable A3-restricted responses during acute infection. Only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 7/8 individuals with acute responses had specific responses for this epitope.
- KIRLRPGGK and RLRPGGKKK were the most commonly recognized HLA-A3 epitopes during acute infection, after 1 year of treatment, and after STI. RLRPGGKKK was immunodominant during acute infection and throughout the study period in the 5/6 individuals who targeted it.

HXB2 Location p17 (20–28)
Author Location Gag (LAI)
Epitope RLRPGGKKK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords class I down-regulation by Nef
References Lewinsohn *et al.* 2002

- CTL kill targets through releasing perforin, that forms pores in the plasma membrane, and granzymes, that induce apoptosis.
- Vpr is capable of arresting infected cells in the G2 phase, and it was hypothesized that Vpr may inhibit CTL-mediated apoptosis because it interacts with the granzyme B molecular complex.
- Vpr expression in the target cell did not inhibit epitope specific lysis – neither perforin or granzyme mediated events were inhibited, as measured by a Chromium release assay and a TUNEL assay.
- In contrast, deletion of Nef, which is thought to protect primary HIV infected cells by down-regulating cell-surface expression of MHC class I complexes, increased the susceptibility of HIV-1 infected cells to CTL mediated killing 2-fold using the TUNEL assay.

HXB2 Location p17 (20–28)
Author Location p17
Epitope RLRPGGKKK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, A11, B35, B51
Keywords mother-to-infant transmission
References Sabbaj *et al.* 2002a

- IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release.
- T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known A3 epitope RLRPGGKKK.
- The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A*0201, A3, B44, B57, Cw5, Cw6; A1, A3, B7, B14, Cw*0702, Cw*0802; A1, A3, B8, B35; A1, A3, B8, B62, Cw3, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- This epitope was recognized in four individuals during early infection, each time presented by A3.
- All HIV-1 proteins except Vpu were recognized, and responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Epitope name A3-RK9 Ga9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant rlrpggkkT. The CTL response declined over time, and the response to the second variant was lower than to the first one throughout.

HXB2 Location p17 (20–28)
Author Location p17 (20–28)
Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 5 epitopes from this individual that varied over time where the internal mutations became fixed; 4/5 epitopes (all except p17 RLRPGGKKK, this eptiope) showed a dramatic decrease in CTL activity against the wild type epitope as the mutation arose. The rlrpggkkR variant was found at 47 and 120 months post-seroconversion.

HXB2 Location p17 (20–28)
Author Location Gag

Epitope RLRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- 0/5 HLA A3+ infection-resistant men, and 0/3 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location p17 (20–28)
Author Location Gag (20–28)
Epitope RPRPGGKKK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Assay type cytokine production, proliferation, CD8 T-cell Elispot - IFNγ, Tetramer binding, Intracellular cytokine staining, Flow cytometric CTL assay
Keywords HAART, ART, memory cells, characterizing CD8+ T cell responses
References Daniel *et al.* 2004

- CD4+ and CD8+ responses in chronically HIV-1 infected patients on HAART were weak with decreased polyclonality. Only 33% of patients had CD4+ T-cells that could proliferate, and only 22% had HIV-specific CD8+ T-cell responses, and those rare responses showed low perforin levels and persistent expression of CD27, indicating incomplete differentiation and loss of lytic function.

HXB2 Location p17 (20–28)
Author Location p17 (20–28 B consensus)
Epitope RLRPGGKKK
Epitope name RK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords immunodominance, escape, acute infection, characterizing CD8+ T cell responses, reversion, viral fitness
References Allen *et al.* 2004

- KK9 and RK9 overlap, are presented by HLA-A3, and are frequently immunodominant and involved in acute-phase primary responses. A mutation in the C-terminal flanking residue of KK9 (K to Q) (kirlrpkkg-Q) inhibits processing of the immunodominant gag KK9 epitope, resulting in rapid decline in the KK9 specific CD8+ T-cell response. At the same time it abrogates the response to RK9 through the embedded mutation rlrpggkQk. Transmission of this mutation to patients expressing HLA-A3 prevents acute-phase response to these epitopes, although the mutation can eventually revert to wild-type allowing a delayed response to the epitope.

HXB2 Location p17 (20–28)
Author Location (B consensus)
Epitope RLRPGGKKK
Epitope name RK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A02, A03, B08, B62, Cw7, Cw10; A01, A03, B08, B14, Cw7, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exhibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 2/9 individuals recognized this epitope, presented by HLA-A3.

HXB2 Location p17 (20–28)
Author Location Gag
Epitope RLRPGGKKK
Epitope name 1332
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3, A3.1, B62, Bw62, B42)
Donor MHC A03, A23, B49, B57, C?; A03, A24, B27, B57, Cw13, Cw18; A03, A26, B08, B52, ?
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, immunodominance, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for RLRPGGKKK: 34% Promiscuous epitope binding to A03, A0301, B62,Bw62, B42. Immunodominant epitope.

HXB2 Location p17 (20–29)
Author Location p17 (20–29 LAI)
Epitope RLRPGGKKKY

Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is an A*0301 epitope.

HXB2 Location p17 (20–29)
Author Location p17 (20–29)
Epitope RLRPGGKKKY
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Goulder *et al.* 2000c
- Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten.
- A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC.

HXB2 Location p17 (20–29)
Author Location p17 (20–29)
Epitope RLRPGGKKKY
Immunogen HIV-1 infection
Species (MHC) human (A3.1)
References Brander & Walker 1995
- Unpublished, C. Jassoy and Beatrice Culman, pers. comm.

HXB2 Location p17 (20–29)
Author Location p17 (20–29 LAI)
Epitope RLRPGGKKKY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3.1)
References Wilkens & Ruhl 1999
- Pers. comm., B. Wilkens and D. Ruhl.

HXB2 Location p17 (20–29)
Author Location p17 (20–29)
Epitope RLRPGGKKKY
Immunogen HIV-1 infection
Species (MHC) human (A30, A3.1)
Keywords immunodominance
References Betts *et al.* 2000
- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was A30, and one was A3, and both responded to RLRPGGKKKY.
- The A2+ A3 individual also reacted with two other A3.1 epitopes.

HXB2 Location p17 (20–29)
Author Location p17 (20–29 IIIB)
Epitope RLRPGGKKKY
Immunogen HIV-1 infection
Species (MHC) human (B42)
Keywords responses in children, mother-to-infant transmission
References Wilson *et al.* 1996
- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.
- RLRPGGKKRY, a naturally occurring variant, was found in non-transmitting mother and is recognized.
- Binds HLA-A3 and Bw62 as well.

HXB2 Location p17 (20–29)
Author Location p17 (20–29)
Epitope RLRPGGKKKY
Immunogen HIV-1 infection
Species (MHC) human (B42, Bw62)
References Ferrari *et al.* 2000
- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p17 (20–29)
Author Location p17 (20–29)
Epitope RLRPGGKKKY
Immunogen HIV-1 infection
Species (MHC) human (B62)
References Brodie *et al.* 2000
- Study tracks and quantifies *in vivo* migration of neo-marked CD8+ HIV-specific CTL.
- Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication.
- The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1α and MIP-1β, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism.
- This study provides a methodology for tracking and studying antigen specific CTL *in vivo*.

HXB2 Location p17 (20–29)
Author Location p17 (20–29 LAI)
Epitope RLRPGGKKKY
Subtype B
Immunogen
Species (MHC) human (Bw62)
Keywords review
References McMichael & Walker 1994
- Review of HIV CTL epitopes.
- Also P. Johnson, pers. comm.

HXB2 Location p17 (20–30)
Author Location p17 (SF2)
Epitope RLRPGGKKKYK
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – the dominant response in a Haitian immigrant living in Boston who was HLA A24/29 B7/B44 Cw6/7 was to this epitope, although the restricting element was not determined.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (20–35)
Author Location p17 (90–105 SF2)
Epitope CLRPGGKKKYKLKHIV
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA A-2, A-24, B-13, B-35.

HXB2 Location p17 (21–35)
Author Location Gag
Epitope LRPGGKKKYKLKHIV
Immunogen HIV-1 infection
Species (MHC) human
References Weekes *et al.* 1999a

- Peptide 703.3: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTL populations.

HXB2 Location p17 (21–35)
Author Location p17 (91–105 SF2)
Epitope LRPGGKKKYKLKHIV
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A1, A2, B50, B57.

HXB2 Location p17 (21–35)
Author Location Gag
Epitope LRPGGKKKYKLKHIV
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords TCR usage
References Weekes *et al.* 1999b

- Peptide 703.3: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population.
- HIV CTL responses to 3 Env and 2 Gag peptides were studied.
- The clonal composition of the TCR Vβ responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.1 and Vβ5.2.

HXB2 Location p17 (21–35)
Author Location p17 (21–35)
Epitope LRPGGKKKYKLKHIV
Immunogen
Species (MHC) human (B8)
References Nixon & McMichael 1991

- Two CTL epitopes defined (see also p24(191-205))

HXB2 Location p17 (21–35)
Author Location p17 (21–35)
Epitope LRPGGKKKYKLKHIV
Immunogen HIV-1 infection
Species (MHC) human (not B8)
References van Baalen *et al.* 1996

- Unknown HLA specificity, but not B8.

HXB2 Location p17 (21–40)
Author Location p17 (21–40 subtype A)
Epitope LRPGGKKKYRLKHLVWASRE
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (Cw4)
Keywords inter-clade comparisons
References Dorrell *et al.* 1999

- CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa.
- This epitope was defined in an A subtype infection – the B clade variant (LRPGGKKKYKLKHIVWASRE) has two mutations relative to the A subtype form, and the CTLs from this patient were not A-B cross-reactive.

HXB2 Location p17 (22–31)
Author Location Gag (22–31)
Epitope RPGGKKRYKL
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Jin *et al.* 2000b

- This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor.
- A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing.

HXB2 Location p17 (24–31)
Author Location p17 (24–31)
Epitope GGKKKYKL
Immunogen
Species (MHC) human (B8)
References Goulder *et al.* 1997g

- The crystal structure of this peptide bound to HLA-B8 was used to predict new epitopes and the consequences of epitope variation.
- The predictions were experimentally confirmed.
- The anchors for HLA-B8 epitopes, as defined by peptide elution data, are P3 (K), P5 (K/R), and P8 (L).
- Structural data suggests that a positive charge at P5 is essential, but that the constraints on P3 may be less severe.
- Small hydrophobic residues at P2 may be favorable for binding.
- A spacious F-pocket favors mid-sized hydrophobic residues in the C-term anchor.

HXB2 Location p17 (24–31)
Author Location p17 (24–31 SF2)
Epitope GGKKKYKL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords inter-clade comparisons
References McAdam *et al.* 1998

- CTL from a patient infected with clade B virus did not recognize Ugandan variants of this epitope.

HXB2 Location p17 (24–31)
Author Location p17 (24–31 LAI)
Epitope GGKKKYKL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords TCR usage
References Reid *et al.* 1996

- The variants 7R: GGKKKYRL, 7Q: GGKKKYQL, 5R: GGKKRYKL, and 3R: GGRKKYKL, were studied.
- Crystal structures were obtained to study these peptides in the context of HLA-B8, and CTL binding and activity were determined.
- 3R has been detected in 3 patients, and it abolishes recognition causing extensive conformational changes upon binding including MHC main chain movement.
- 7Q and 7R alter the TCR exposed surface, and retain some recognition.
- Reactivity of 5R depends on the T cell clone, this amino acid is embedded in the C pocket of B8 when the peptide is bound.
- Optimal peptide is 8-mer, not 9-mer, and positions 3, 5, and 8 are the anchor residues.

HXB2 Location p17 (24–31)
Author Location p17 (24–31 LAI)
Epitope GGKKKYKL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Price *et al.* 1997

- A weak CTL response to the index peptide was observed in an HLA-B8+ infected individual.
- Sequences from the earliest available time point showed that a variant at position 5, an anchor residue, GGKKQYKL, was present.

HXB2 Location p17 (24–31)
Author Location p17
Epitope GGKKKYKKL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART
References Seth *et al.* 2001

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.

HXB2 Location p17 (24–31)
Author Location p17 (24–31 SF2)
Epitope GGKKKYKL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 1/3 group 2, and 2/2 group 3.

HXB2 Location p17 (24–31)
Author Location p17 (24–31)
Epitope GGKKKYRL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B8)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location p17 (24–31)
Author Location p17 (24–31)
Epitope GGKKKYKL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Day *et al.* 2001

- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.

HXB2 Location p17 (24–31)
Author Location p17
Epitope GGKKKYKL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords binding affinity, review, inter-clade comparisons, epitope processing, escape
References McMichael & Hanke 2002

- CTL response-eliciting vaccines are reviewed. The natural epitope interactions with the HLA class I presenting molecules and T-cell receptors are described, using the structure of this epitope, taken from Reid *et al.* [1996], as an example.

HXB2 Location p17 (24–31)
Author Location (B consensus)
Epitope GGKKKYKL
Epitope name GL8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A01, A03, B08, B14, Cw7, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location p17 (24–32)
Author Location p17 (24–32 LAI)
Epitope GGKKKYKLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes epitope to be presented by B*0801.

HXB2 Location p17 (24–32)
Author Location p17 (24–32 LAI)
Epitope GGKKKYKLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Sutton *et al.* 1993

- Exploration of HLA-B8 binding motif through peptide elution.

HXB2 Location p17 (24–32)
Author Location p17 (24–32 LAI)
Epitope GGKKKYKLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords epitope processing
References Rowland-Jones *et al.* 1993

- Study of an individual with partially defective antigen processing.

HXB2 Location p17 (24–32)
Author Location p17 (24–32)
Epitope GGKKKYKLK
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Klenerman *et al.* 1994

- Naturally occurring variants GGKKKYQLK and GGKKRYRLK may act as antagonists.

HXB2 Location p17 (24–32)
Author Location p17 (24–32)
Epitope GGKKKYKLK
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Klenerman *et al.* 1995

- Naturally occurring antagonist GGKKKYQLK found in viral PBMC DNA and RNA.

HXB2 Location p17 (24–32)
Author Location p17 (24–32)
Epitope GGKKKYKLK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords escape
References Nowak *et al.* 1995

- Longitudinal study of CTL response and immune escape – the variant GGRKKYKLK binds to HLA-B8 but is not reactive.

HXB2 Location p17 (24–32)
Author Location p17 (24–32)
Epitope GGKKKYKLK
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Dyer *et al.* 1999

- CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 that was Nef-defective.
- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.

HXB2 Location p17 (24–32)
Author Location p17
Epitope GGKKKYKLK
Immunogen
Species (MHC) human (B8)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective.
- HIV-2 sequence: GGKKKYKMK – no cross-reactivity Phillips *et al.* [1991].

HXB2 Location p17 (24–32)
Author Location p17 (24–32)
Epitope GGKKKYKLK
Epitope name GGK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- This epitope was recognized by 1/7 study subjects that were HLA-B8+.
- Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy.

HXB2 Location p17 (24–32)
Author Location p17
Epitope GGKKKYKLK
Epitope name GGK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location p17 (24–35)
Author Location p17 (25–35 SF2)
Epitope GGKKKYKLKHIV
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords review, immunodominance, escape
References Goulder *et al.* 1997a; Phillips *et al.* 1991

- Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time.
- Goulder *et al.* [1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA-B27 patients.

HXB2 Location p17 (24–35)
Author Location p17 (25–35)
Epitope GGKKKYKLKHIV
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Birk *et al.* 1998b

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (28–36)
Author Location
Epitope KYRLKHLVW
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls (ML1573).

HXB2 Location p17 (28–36)
Author Location (C consensus)
Epitope HYMLKHLVW
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*2301, A*2402)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression was also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.

- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p17 (28–36)
Author Location p17 (28–36 LAI)
Epitope KYKLKHIVW
Subtype B
Immunogen
Species (MHC) human (A*2402)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes that this is an A*2402 epitope.

HXB2 Location p17 (28–36)
Author Location p17 (28–36 SF2)
Epitope KYKLKHIVW
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1998

- Strong CTL activity to this peptide was detected in 2/3 HIV-infected individuals who were HLA A24+.
- HLA A24 is very common in Japanese (70% carry it) and is common globally.
- This epitope was detected by looking for peptides with appropriate A24 anchor residues (Y at position 2, carb-term ILF or W) – 16/17 such peptides bound to A24 – KYKLKHIVW was found to be a naturally processed epitope that elicits a strong CTL response.

HXB2 Location p17 (28–36)
Author Location p17 (28–36 LAI)
Epitope KYKLKHIVW
Subtype B
Immunogen
Species (MHC) human (A23)
References Goulder & Walker 1999

- P. Goulder, pers. comm.

HXB2 Location p17 (28–36)
Author Location p17 (28–36 LAI)
Epitope KYKLKHIVW
Subtype B
Immunogen
Species (MHC) human (A24)
References Brander & Walker 1996

- D. Lewinsohn, pers. comm.

HXB2 Location p17 (28–36)
Author Location p17 (28–36 SF2)
Epitope KYKLKHIVW
Immunogen HIV-1 infection
Species (MHC) human (A24)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A24+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 2/3 group 2, and 0/0 group 3.

HXB2 Location p17 (28–36)
Author Location p17 (28–36 93TH253 subtype CRF01)
Epitope KYKLKHIVW
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A24)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- The only HLA-A24 FSWs tested did not recognize the E clade version of this epitope KYKMKHLVW, which differs from the previously defined B clade version by two amino acids, KYKLKHIVW.

HXB2 Location p17 (28–36)
Author Location p17
Epitope KYKLKHIVW
Epitope name KW9
Immunogen HIV-1 infection
Species (MHC) human (A24)
Donor MHC A2, A24 B38, B60, Cw2, Cw12
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), acute infection
References Montefiori *et al.* 2003

- HIV-1 + patient AC10 underwent early HAART treatment, which was discontinued 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.

HXB2 Location p17 (28–36)
Author Location p17 (28–36)
Epitope KYKLKHIVW

Immunogen HIV-1 infection
Species (MHC) human (A24)
Donor MHC A0201/2402, B52/75, Cw3; A0207/2402, B46/52, Cw1; A2402/26, B7/5101, Cw7
Country Japan.
Assay type Chromium-release assay
Keywords epitope processing, escape
References Yokomaku *et al.* 2004

- Epitope variants escaped from being killed by CTLs in an endogenous expression system although they were recognized when corresponding synthetic peptides were exogenously loaded onto the cells. Escape is thus probably due to changes that occur during the processing and the presentation of epitopes in infected cells.
- Epitope variants recognized when added exogenously but not when processed endogenously were: kyRlkhLvw, RyRlkhLvw and QyRlkhivw.

HXB2 Location p17 (28–36)
Author Location p17 (728–736 subtype A)
Epitope KYRLKHLVW
Subtype A
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (Cw4)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-Cw4 women, 2/2 HEPS and 7/11 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in both of the 2/2 HEPS cases and in 3 of the 7/11 HIV-1 infected women.

HXB2 Location p17 (28–36)
Author Location p17 (28–36)
Epitope KYRLKHLVW
Immunogen HIV-1 infection
Species (MHC) human (Cw4)
References Appay *et al.* 2000

- This epitope is newly defined in this study.
- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α.

HXB2 Location p17 (33–41)
Author Location p17
Epitope HLVWASREL
Epitope name HL-9
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (Cw*0804)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, epitope processing, immunodominance, cross-presentation by different HLA
References Masemola *et al.* 2004b

- Highly targeted regions in Gag for CD8+ T-cells were defined for individuals with C clade infections in South Africa. Nine specific epitopes within the most reactive regions were characterized. This is one of five novel epitopes that were found among subtype C HIV-1 from African patients that hadn't previously been identified in B clade infections. Some epitopes were shown to be promiscuous, presented by multiple class I restricting alleles.
- HLVWASREL was presented by Cw*08 and newly identified in this study; Cw*08 is slightly more common in Zulus than Caucasians (0.066 versus 0.038).

HXB2 Location p17 (34–44)
Author Location p17
Epitope LVWASRELERF
Epitope name LF-11
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*3002, B*570301)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, epitope processing, immunodominance, cross-presentation by different HLA
References Masemola *et al.* 2004b

- Highly targeted regions in Gag for CD8+ T-cells were defined for individuals with C clade infections in South Africa. Nine specific epitopes within the most reactive regions were characterized. This is one of five novel epitopes that were found among subtype C HIV-1 from African patients that hadn't previously been identified in B clade infections. Some epitopes were shown to be promiscuous, presented by multiple class I restricting alleles.
- LVWASRELERF was clearly presented by both A*3002 and B*570301, it might also be cross-presented by A*3001, but not as effectively. A*30 is ten fold more common among Zulus than Caucasians (allele frequency 0.195 versus 0.019), while B*57 is roughly comparable (0.051 versus 0.043).

HXB2 Location p17 (34–44)
Author Location (C consensus)
Epitope LVWASRELERF
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p17 (36–44)
Author Location p17 (SF2)
Epitope WASRELERF
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The dominant response in an African American who was HLA A3/33 B35/B53 Cw4/7 was to this epitope, although the restricting element was not determined – this epitope fell outside the most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (36–44)
Author Location p17 (35–43 LAI)
Epitope WASRELERF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Goulder *et al.* 1997d

- Optimal epitope defined from within p17(30-44), LKHIVWASRELERFA.
- Dominant CTL response in an HIV+ asymptomatic donor was to this epitope.
- The Phe in the C-term anchor is distinct from the previously-defined Tyr for B*3501 C-term anchors.

HXB2 Location p17 (36–44)
Author Location p17 (36–44 LAI)
Epitope WASRELERF
Subtype B
Immunogen
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004; Goulder *et al.* 1997b

- C. Brander notes this is a B*3501 epitope.

HXB2 Location p17 (36–44)
Author Location p17 (36–44)
Epitope WASRELERF
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Birk *et al.* 1998b

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (36–44)
Author Location p17 (36–44)
Epitope WASRELERF
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p17 (36–44)
Author Location p17 (36–44 SF2)
Epitope WASRELERF
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3.

HXB2 Location p17 (36–44)
Author Location
Epitope WASRELERF
Epitope name Gag-WF9
Subtype B
Immunogen HIV-1 infection

Species (MHC) human (B35)
References Sabbaj *et al.* 2002b
- Among HIV+ individuals who carried HLA B35, 1/21 (5%) recognized this epitope.

HXB2 Location p17 (36–44)
Author Location Gag
Epitope WASRELERF
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004
- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- No one, 0/3 HLA B35+ infection-resistant men, and 0/5 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location p17 (69–93)
Author Location p17 (69–93 BH10)
Epitope QTGSEELRSLYNTVATLYCVHQRIE
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Johnson *et al.* 1991
- Gag CTL response studied in three individuals.

HXB2 Location p17 (71–79)
Author Location p17 (71–79 LAI)
Epitope GSEELRSLY
Subtype B
Immunogen
Species (MHC) human (A1)
References Brander & Walker 1996
- P. Goulder, pers. comm.

HXB2 Location p17 (71–79)
Author Location p17 (71–79)
Epitope GSEELRSLY
Immunogen HIV-1 infection
Species (MHC) human (A1)
References Birk *et al.* 1998b
- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (71–79)
Author Location p17 (71–79 HXB2)
Epitope GSEELRSLY
Epitope name GSE
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A1)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, acute infection
References Oxenius *et al.* 2000
- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- This epitope was not recognized by the 6/8 study subjects that were HLA-A1.

HXB2 Location p17 (71–79)
Author Location p17 (71–79)
Epitope GSEELRSLY
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A1)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-A1 women, 1/1 HEPS and 3/3 HIV-1 infected women recognized this epitope, and the response was the dominant HLA-A1 response in all cases.

HXB2 Location p17 (71–79)
Author Location p17
Epitope GSEELRSLY
Epitope name GSE
Immunogen HIV-1 infection
Species (MHC) human (A1)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b
- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with supervised treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location p17 (71–79)
Author Location p17 (71–79)

Epitope GSEELRSLY
Immunogen HIV-1 infection
Species (MHC) human (A1)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 3/13 patients recognized this epitope.

HXB2 Location p17 (71–79)
Author Location (71–79 B consensus)
Epitope GSEELRSLY
Epitope name GY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A1)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords characterizing CD8+ T cell responses
References Allen *et al.* 2004

- This study characterizes an escape mutation in a C-terminal flanking residue of the HLA-A3 gag p17 KK9 epitope that inhibits processing, and is embedded in the overlapping HLA-A3 RK9 epitope.
- The immune response was tracked in subject AC-38. The acute immunodominant response was to the B57 TW10 epitope; this response declined following viral escape (tsNlqeqigw) by day 64. The p17 KK9 and RK9 became immunodominant, but then declined as the escape mutation arose. Three other strong responses that persisted were detected, along with one subdominant response to GY9.

HXB2 Location p17 (71–85)
Author Location p17 (71–85 SF2)
Epitope GSEELRSLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A1, A11, B8, B27.

HXB2 Location p17 (71–85)
Author Location p17 (71–85 HXB2)
Epitope GSEELRSLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 were chronically infected and treated; 22 started treatment during acute infection; 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p17 (71–90)
Author Location Gag (HXB2)
Epitope GSEELRSLYNTVATLYCVHQ
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A2
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement, HAART, ART
References Chitnis *et al.* 2003

- 17 perinatally HIV-1 infected children (0.08-16 years) were evaluated for HLA-A2-restricted IFN-gamma CD8+ CTL responses against 4 immunodominant peptides that carry HLA-A2 epitopes. Two peptides were from gp120 (one at position 112, one from the V3 loop), and one each was from gp41 and Gag. 15/17 patients responded to the Gag peptide, 13/17 to the gp41 and the non-V3 gp120 peptides, and 11/17 responded to the V3 loop. 4 children recognized all 4 peptides.
- In 10/14 children, addition of exogenous IL-15 induced increased frequencies of SFCs to the Gag peptide. IL-2 and IL-7 did not increase SFCs, however IL-2, IL-7 and IL 15 could all increase the intensity of the spots in some patients. In 4 children, IL-15 addition brought the SFC response up to the level of detection.

HXB2 Location p17 (74–82)
Author Location p17
Epitope ELRSLYNTV
Immunogen
Species (MHC) human (B*0801)
Keywords optimal epitope
References Frahm *et al.* 2004

- Noted by Brander to be a B*0801 epitope.

HXB2 Location p17 (74–82)
Author Location p17
Epitope ELRSLYNTV
Immunogen
Species (MHC) human (B8)
References Goulder *et al.* 1997g
- Defined in a study of the B8 binding motif.

HXB2 Location p17 (74–82)
Author Location p17 (74–82)
Epitope ELRSLYNTV
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Birk *et al.* 1998b
- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (74–82)
Author Location p17 (74–82)
Epitope ELRSLYNTV
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Ferrari *et al.* 2000
- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p17 (74–82)
Author Location p17 (74–82)
Epitope ELRSLYNTV
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Day *et al.* 2001
- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.

HXB2 Location p17 (74–82)
Author Location (B consensus)
Epitope ELRSLYNTV
Epitope name EV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A11, A29, B08, B44, Cw4, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c
- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location p17 (74–83)
Author Location Gag
Epitope ELRSLYNTVA
Epitope name 1241
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003
- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for ELRSLYNTVA: 71%. This epitope was previously identified in the literature, but was not confirmed in this study.

HXB2 Location p17 (76–86)
Author Location p17 (74–86 LAI)
Epitope RSLYNTVATLY
Subtype B
Immunogen
Species (MHC) human (A*3002)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is an A*3002 epitope.

HXB2 Location p17 (76–86)
Author Location p17 (SF2)
Epitope RSLYNTVATLY
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a
- The CTL-dominant response was focused on this epitope in a single HIV+ individual from Boston – this epitope fell outside the most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (76–86)
Author Location Gag (96ZM651.8)
Epitope RLSYNTVATLY

Immunogen
Species (MHC) human (A*3002)
References Novitsky *et al.* 2001

- This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort.
- Only 3/13 (23.1%) A*3002-positive subjects demonstrated moderate CTL responses to the peptide GTEELRSLYNTVATLYCVHE (residues 71 to 90), which contains the previously described A*3002 epitope RLSYNTVATLY.

HXB2 Location p17 (76–86)
Author Location p17 (76–86)
Epitope RSLYNTVATLY
Epitope name RY11 (p17)
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
References Goulder *et al.* 2001a

- HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule.
- A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood.
- Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean.
- In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant.
- Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41).
- HLA-A*3001-positive targets do not present RSLYNTVATLY.

HXB2 Location p17 (76–86)
Author Location
Epitope RSLYNTVATLY
Epitope name Gag-RY11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Donor MHC A*3002 A*3201 B*4501 B*5301 Cw*0401 Cw*1202
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes YPLTFGWCY, Nef(135-143), HLA B*5301; AETFYVDGA, RT(437-445), HLA B*4501; and HIGPGRAFY, gp160(310-318), HLA A*3002.
- Among HIV+ individuals who carried HLA B30, 3/16 (19%) recognized this epitope.

HXB2 Location p17 (76–86)
Author Location (C consensus)
Epitope RSLYNTVATLY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p17 (76–86)
Author Location p17 (74–86 SF2)
Epitope RSLYNTVATLY
Immunogen HIV-1 infection
Species (MHC) human (A30)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with preseroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A30+ individuals that had a CTL response to this epitope broken down by group: 0/1 group 1, 0/0 group 2, and 1/1 group 3.

HXB2 Location p17 (76–86)
Author Location p17
Epitope RSLYNTVATLY
Epitope name A30-RY11(p17)
Subtype B

Immunogen HIV-1 infection
Species (MHC) human (A30)
Donor MHC A30, A32, B18, B27
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8+ T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).

HXB2 Location p17 (76–86)
Author Location p17
Epitope RSLYNTVATLY
Epitope name RY-11
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A30)
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, epitope processing, immunodominance, cross-presentation by different HLA
References Masemola *et al.* 2004b

- Highly targeted regions in Gag for CD8+ T-cells were defined for individuals with C clade infections in South Africa. Nine specific epitopes within the most reactive regions were characterized.
- RSLYNTVATLY was presented by A*30, which is more common in Zulus than Caucasians (0.195 versus 0.019). This epitope had previously identified in B clade infections.

HXB2 Location p17 (76–86)
Author Location p17
Epitope RSLYNTATLY
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A30)
Donor MHC A02, A30, B4402, B15
Assay type T-cell Elispot
Keywords HIV exposed persistently seronegative (HEPS)
References Missale *et al.* 2004

- HIV-specific T-cell response was tested in HIV-uninfected patients exposed to blood from a patient with highly replicating HIV; these same patients were nosocomially infected with HBV. HIV-specific T-cell responses were directed to structural and non-structural HIV proteins in two patients suggesting that the virus replicated in these patients sufficiently to prime a cell-mediated immune response that protected these individuals from HIV infection.
- This patient responded to 4/8 HIV epitopes tested in an IFNgamma elispot assay or tetramer assay. Responses were detected 8 and 28 weeks after exposure, this particular epitope was only tested with elispot.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human
Keywords review, escape
References Sewell *et al.* 2000

- Review of the impact of CTL on viral immunity and escape that notes that SLYNTVATL-tetramer binding cells in individuals that react to this epitope inversely correlate with plasma viral load.

HXB2 Location p17 (77–85)
Author Location (SF2, HXBc2/Bal chimeric)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC)
Keywords rate of progression, escape
References Douek *et al.* 2002

- Seven HIV-positive subjects tended to make their strongest CD8+ T-cell response against Gag; these responses had varying breadth and magnitude that were unrelated to disease progression.
- Patient TX7 primarily recognized SL9 during a three year study period and used six T-cell clonotypes for this recognition.
- SLYNTVATL was the only form of the epitope found initially, but three alternate forms eventually appeared: SLYNTVAVL, SLYNTIATL, and most commonly SLYNTIAVL. These distinct forms bind A2, but have distinct abilities to stimulate different T-cell clonotypes.
- In subject TX7, the observed mutations of SL9 failed to escape overall CTL recognition, presumably because the six T-cell clonotypes allowed a more flexible response.
- The BV17 T-cell clone recognized SL9 but not SLYNTIAVL, and BV17 became undetectable at week 20 when SLYNTIAVL predominated. Subsequently BV17 became the second most common clone. Thus the relative frequency of the T-cell clonotypes varied with respect to each other and to epitope variation.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)

Epitope SLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*0201
Keywords HAART, ART, responses in children
References Luzuriaga *et al.* 2000

- Longitudinal study of 8 infants with prolonged viral suppression due to combination antiretroviral therapy showed no HIV-1 specific CTL responses in peripheral blood cells. 6/8 were studied using a Chromium release assay and no response was detected using Gag expressed in vaccinia in the target cells. Three HLA-A*0201 children were tested using SLYNTVATL or ILKEPVHGV HLA A*0201 tetramers and again no HIV-specific response was detected, either using PBMC specimens, or PBMC which had been stimulated *in vitro* for a week.
- In contrast, one of the children with therapy suppressed HIV viral replication who was co-infected with HIV and EBV, while HIV-tetramer negative, had EBV-tetramer staining cells at a frequency of 0.14% in the PBMC.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords HAART, ART
References Huang *et al.* 2000

- The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed.
- Increases in gamma IFN producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT.
- 4/8 A*02 subjects had a positive response to this epitope indicating that it is a major epitope for CD8+ gamma IFN production.
- In 3/3 HLA A*02, B*27 individuals, the dominant response in gag measured by both gamma IFN production and T-cell lysis was a B27 epitope, p24(263-272), not the A2 SLYNTVATL epitope.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords HAART, ART
References Rinaldo *et al.* 2000

- Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that can persist after therapy and long periods of virus being below the level of detection.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords HAART, ART, immunodominance
References Scott-Algara *et al.* 2001

- This study examined with CTL response in HLA A*02+ children by tetramer staining for HLA-A2 immunodominant epitopes SLYNTVATL and ILKEPVHGV.
- 71% of the 28 HIV-1 infected HLA-A*02 positive children recognized both epitopes, with cells from 26 children stained positive by the gag tetramer (SLYNTVATL) and 21 children by the pol tetramer (ILKEPVHGV)
- There were no differences observed in children that had therapy versus those that did not.
- Tetramer-binding cells were memory activated CD28-, CD45RO+, CD45RA- HLADR+, CD69-, CD8+ T-cells.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 HXB2)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords epitope processing, immunodominance, escape
References Brander *et al.* 1999

- Multiple natural variations in the SL9 flanking regions of the immunodominant epitope SLYNTVATL were tested and found not to adversely affect CTL recognition or prevent epitope processing, suggesting that viral escape from the HLA-A*0201-restricted CTL response against SLYNTVATL is probably not linked to variations in the flanking regions of this epitope.
- The substitution Y79F was an escape mutation in that it interfered with CTL recognition by one CTL clone from an A*0201 infected individual, clone 13010.B17, but it was still recognized by another CTL clone, 115.D4.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T-cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.

- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location p17 (77–85)
Author Location Gag
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Tan *et al.* 1999

- Adoptive transfer of two autologous *in vitro*-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- Individuals who did not respond to SLYNTVATL recognized other HIV epitopes, and 2/4 SLYNTVATL responders had stronger responses to epitopes restricted by other class I alleles.
- SLYNTVATL was the only response detected in a one individual that was HLA A*0201, B44, B70.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART
References Ogg *et al.* 1999

- CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SLYNTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient.
- Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy.
- After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Altman *et al.* 1996

- This paper introduces the tetramer methodology that permits quantification of specific CTL based on expression of specific TCRs – HLA-A2 tetramers were prepared that can stain CTL lines specific for ILKEPVHGV and SLYNTVATL, and quantitate HIV-specific CD8+ cell lines in freshly isolated PBMCs.
- Three patients only stained the Gag epitope SLYNTVATL, one patient had the highest frequency of tetramer staining to the Pol epitope (0.77%), less to the Gag epitope (0.28%).

HXB2 Location p17 (77–85)
Author Location Gag
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART
References Gray *et al.* 1999

- Administration of highly active antiretroviral therapy (HAART) reduced CD8+ cell frequency, and the CD8+ cells detected by tetramer staining were likely to be memory cells, indicating that persistently replicating viral populations are needed to maintain high frequencies of HIV-1 specific CTL.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 SF2)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords inter-clade comparisons
References McAdam *et al.* 1998

- CTL from a patient infected with clade B virus did not recognize the clade A analog of this epitope.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords TCR usage
References Wilson *et al.* 1998a

- HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed *in vivo*.
- Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls.
- Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases.
- An A2-Gag specific line from one patient was found to be BV8, and at its highest level represented 17.5% of the patient's CD8+ T cells.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Ogg *et al.* 1998b

- HLA-tetrameric complexes were used in a cross-sectional study of 14 untreated HLA A*0201 positive individuals, revealing an inverse relationship between HIV Gag and Pol specific CTL effector cells (CTLe) and viral load.
- Inclusion of both the p17 SLYNTVATL and RT ILKEPVHGV epitopes gives a good representation of HLA A*0201-restricted activity.
- No correlation was observed between the CTLe and CD4 count or clearance rate of productively infected cells.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords epitope processing
References Walter *et al.* 1997

- HLA-A2 heavy chain and β2-microglobulin expressed in E. coli were refolded in the presence of this peptide.
- The HLA-A2-peptide complex elicited HLA-A2 peptide-specific CTL response in cells lacking HLA-A2.
- Suggests that preformed HLA-peptide complexes could provide an alternate to intracellular processing for immunogens.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Lalvani *et al.* 1997

- A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers.
- This peptide was one of the test peptides for optimizing the protocol.

HXB2 Location p17 (77–85)
Author Location p17 (76–84)
Epitope SLYNTVATL
Epitope name SL9
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
References van der Burg *et al.* 1996

- Slow dissociation rate is associated with immunogenicity.
- CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords review, escape
References Goulder *et al.* 1997e; Goulder *et al.* 1997a

- HLA-identical siblings, hemophiliac brothers, were both infected with the same batch of factor VIII.
- One had a response to gag A2 epitope SLYNTVATL, the other to pol A2 epitope ILKEPVHGV. They were tested 6-8 years after infection.
- Viral sequencing from the twin that had no response to SLYNTVATL indicated his virus had the substituted form SLHNAVAVL.
- 71% of an additional set of 22 HIV-1 infected HLA-A*0201 positive donors preferentially responded to gag SLYNTVATL.
- Those individuals with a pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL.
- An additional subject went from SLYNTVATL responder to non-responder coincident with a switch to the variant SLFNTVATL.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords review
References Goulder *et al.* 1997a

- This paper is a review of CTL and immune evasion, but it presents a study of a shift from an HLA-A*0201 response to SLYNTVATL, to a B62 response to GLNKIVRMY.
- As long as a strong CTL response to SLYNTVATL was evident, the epitope variants SLFNTVATL or SLYNTIATL dominated the viral population – eventually the CTL response to the index peptide became undetectable, the CTL response shifted to a focus on GLNKIVRMY, and the index peptide SLYNTVATL once again established itself as the dominant form.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART
References Gray *et al.* 1999

- Peptide-tetramer complexes of A*0201 and SLYNTVATL or ILKEPVHGV were used to study individuals receiving HAART to determine the frequency of Class I HLA-restricted anti-HIV CD8+ T cells.
- 17/18 asymptomatic patients had a CTL response to one or both epitopes – 72% had a CTL response to SLYNTVATL.
- After HAART, the majority of the epitope-specific CTL were apparently memory cells.

HXB2 Location p17 (77–85)

Author Location p17 (77–85 subtype A)
Epitope SLFNTVATL
Epitope name SL9
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords inter-clade comparisons
References Dorrell *et al.* 1999

- CTL responses in three individuals with non-clade B infections were studied, two with subtype A infections, one with subtype C – their infections all originated in East Africa.
- This epitope is most commonly SLYNTVATL in B subtype, and CTL from the C subtype infection did not recognize B clade gag or the 3Y form of the epitope, but did recognize the predominant A and C clade form, SLFNTVATL.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords immunodominance
References Brander *et al.* 1998a

- Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope.
- Only one subject had CTL against all three epitopes.
- There was significant heterogeneity in the CTL response to this immunodominant epitope.
- The overall variation in this epitope among the 17 who had a CTL response and 11 non-HLA A*0201 HIV-1 + individuals was similar, suggesting a lack of immune pressure.
- Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 HXB2)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords rate of progression, immunodominance
References Hay *et al.* 1999

- CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201.
- The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted.
- Despite the initial narrow response to two epitopes, no other CTL responses developed.
- No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak.
- A variant of this epitope was observed *in vivo* (–F—-V-), but this mutation is recognized by SLYNTVATL-specific CTL, and in this case the patient's cells could present the peptide to SLYNTVATL-specific CTL.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART
References Kalams *et al.* 1999b

- Two patients were followed before and after HAART – reduced plasma HIV-1 RNA levels resulted in a decline in HIV-specific in-vivo activated CTL such that by day 260 CTL activities were undetectable.
- ERYLKDQQL was the dominant response in one of the individuals, SLYNTVATL subdominant.
- Sporadic breakthrough in viremia resulted in transient increases in CTLp.
- Memory CTL frequency directed against Vac-Gag, Vac-RT, Vac-Env, and Vac-Nef initially increased with HAART and then decreased with the decline of the viral load.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Spiegel *et al.* 2000

- High levels of CD8+ HIV-1 specific and cytomegalovirus specific CTL were detected by HLA-A*0201-peptide tetramers in 3 infected subjects with very low CD4 counts, but CD8 T cell mediated effector activity was not seen.
- Thus HIV-1 specific CD8+ cells may be present but may lack direct effector activity in late disease, suggesting that overcoming antigen unresponsiveness may be a useful therapeutic strategy.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Larsson *et al.* 1999

- ELISPOT was used to assay the CD8+ T-cell response to the HIV-1 proteins Gag, Pol, Nef or Env expressed in vaccinia vectors in 19 HIV+ people.
- The highest CTL frequency was directed at epitopes Pol.
- In A*0201 individuals, higher numbers of spot-forming T cells were directed against HIV-1 proteins expressed in vaccinia than to peptides SLYNTVATL and ILKEPVHGV presented by A2.

HXB2 Location p17 (77–85)
Author Location p17 (SF2)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)
Epitope SLYNTVATL
Subtype B
Immunogen
Species (MHC) human (A*0201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0201 epitope.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 SF2)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords escape, acute infection
References Goulder *et al.* 2001a

- This epitope is targeted by 75% of HLA-A*0201, HIV+ adults, and the magnitude of the response is inversely correlated with viral load.
- CTL responses to SL9 and autologous SL9 variants were not detected in 11 HLA-A*0201 positive subjects during acute infection.
- Longitudinal studies of two individuals (AC13 and PI004) showed that the initial control of viremia was independent of the SL9 CTL response.
- Low Gag expression levels did not correlate with the delayed CTL response to this epitope.
- Autologous SL9 variants SLYNTIAVL, SLYNTVAVL, SLFNTVATL, SLFNTVATL, and SLFNTVATL are each capable of inducing a range of CTL responses, sometimes strong, sometimes diminished, and sometimes complete escape relative to the wild type variant SLYNTVATL in patients with chronic HIV-1 infection – the ability to cross-react with a particular variant was patient dependent.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Epitope name p17 SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, including p17 SL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2).
- p17 SL9 was recognized in 12/22 patients with chronic HIV-1 infection.
- Only 1/13 patients with acute HIV-1 infection recognized p17 SL9.

HXB2 Location p17 (77–85)
Author Location Gag
Epitope SLYNTVATL
Epitope name (SL9)
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Goepfert *et al.* 2000

- This paper describes a comparison of results of different CTL assays, a SL9 tetramer assay and IFN-gamma ELISPOT, using 7 HIV-positive patients.
- The IFN-gamma ELISPOT assay was compared using the single SL9, a pool of overlapping 20 mers, and recombinant vaccinia encoding Gag as antigen – pooled peptides gave the highest number of spot forming cells, vaccinia gave high background.
- A correlation with results of the tetramer assay was found only for ELISPOT using the Gag epitope as antigen, but the tetramer assay detected a 10-fold higher number of cells than could produce IFN-gamma in the ELISPOT assay – the authors suggest not all tetramer-positive cells may produce IFN-gamma, some may be undergoing apoptosis, some may be producing other cytokines.
- The tetramer assay could detect a reaction to SLYNTVATL in most of the HLA-A*0201 chronically HIV-1 infected study subjects.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Immunogen
Species (MHC) human (A*0201)
Keywords binding affinity
References Sandberg *et al.* 2000

- This epitope served as a positive control in a study comparing peptide binding affinity to HLA-A201 to CTL responses upon vaccination with a nef DNA vaccine.

HXB2 Location p17 (77–85)
Author Location Gag (LAI)
Epitope SLYNTVATL
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)

Keywords dendritic cells
References Engelmayer *et al.* 2001

- Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis through *in vitro* by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors.
- Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific CD4+ helper T-cell responses.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)
Epitope SLYNTVATL
Epitope name G3
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using tetramer staining or CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location p17 (77–85)
Author Location Gag
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Gea-Banacloche *et al.* 2000

- In a study including many long-term non-progressors, no correlation between plasma virus levels and number of HIV-specific CD8+ T-cells was found.
- High frequencies of circulating CD8+ T-cells were HIV-1 specific, and the majority of these responses were to gag-pol gene products.
- 4/21 subjects were HLA-(A*0201), and of these only 2 subjects (patient 3 and 19) tested positive to this epitope.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 SF2)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- Tetramer staining with A2, beta2microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific sells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART, rate of progression
References Jin *et al.* 2000a

- The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay.
- LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Appay *et al.* 2000

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Goulder *et al.* 2000b

- Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]).

- HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords dendritic cells
References Ostrowski *et al.* 2000

- The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*.
- Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9/10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients.
- Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes.
- The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE).

HXB2 Location p17 (77–85)
Author Location
Epitope SLYNTVATL
Subtype B
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost, canarypox prime with gp160 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Nef, Pol
Species (MHC) human (A*0201)
Keywords vaccine-specific epitope characteristics
References Ferrari *et al.* 2001

- Different HIV strains were used for different regions: gp41 LAI, Gag LAI, gp120 MN, gp120 SF2.
- Two vaccinees with Gag responses were HLA-A*0201+, but neither made SLYNTVATL responses to the Gag vaccine, in contrast to its frequent recognition in natural infections. No HLA-A*0201 responses were observed to an Env vaccine.

HXB2 Location p17 (77–85)
Author Location
Epitope SLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords rate of progression, immunodominance
References Migueles & Connors 2001

- CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.
- CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia.
- The HLA-A*0201 SLYNTVATL epitope response was not as strong in individuals that carried both A2 and B57.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords epitope processing, immunodominance
References Sewell *et al.* 2002

- Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. 174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing.
- ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.

HXB2 Location p17 (77–85)
Author Location Gag (ADA)
Epitope SLYNTVATL
Epitope name SL-9
Subtype B
Immunogen HIV-1 infected monocyte-derived
Species (MHC) mouse (A*0201)
References Poluektova *et al.* 2002

- Nonobese diabetic NOD-C.B-17 SCID mice were reconstituted with HLA-A*0201 positive human PBL and injected with HIV-1 infected monocyte-derived macrophages MDM in the basal ganglia to provide a mouse model of HIV-1 encephalitis.
- HLA-A*0201 CTL responses were detected by tetramer staining in the spleen in seven days, increased through day 14, and the numbers of productively infected were reduced >85% in the second week.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen computer prediction
Species (MHC) (A*0201)
Keywords inter-clade comparisons, computational epitope prediction, vaccine-specific epitope characteristics, escape
References Schönbach *et al.* 2002

- Computational methods (artificial neural networks [ANN], hidden Markov models [HMM], binding matrices based on HLA association rates BIMAS) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.

- The SLYNTVATL epitope received focused discussion. SLYNTVATL, slFntvatl, slyntvaVl, and slyntIaVl are all recognized variants, ANN predicts all four variants would be recognized, while BIMAS only predicts SLYNTVATL and slFntvatl would be recognized. However, Sewell *et al.* [1997] suggested certain substitutions may be antagonistic, including slFntvatl, and vaccines do not stimulate SLYNTVATL responses as well as natural infections. The authors note these kinds of issues complicate the application of computational predictions of epitopes to vaccine design.

HXB2 Location p17 (77–85)
Author Location Gag (76–84)
Epitope SLYNTVATL
Subtype B
Immunogen Vaccine
Vector/Type: DNA *HIV component:* HIV-1
Species (MHC) mouse (A*0201)
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance
References Singh *et al.* 2002; Sykes & Johnston 1999

- C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome.
- A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members.
- Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV (Pol), RIQRGPGRAFVTIGK (Env) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen.
- The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.

HXB2 Location p17 (77–85)
Author Location
Epitope SLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Donor MHC A0202/2501, B1801/62, C10/1203, DRB1 1501, DQB1 8
Keywords rate of progression, Th1, Th2
References Imami *et al.* 2002b

- 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile. Long term non-progressors had much stronger Th responses, particularly to p24 peptides, and they tended to be balanced between Th1, IL-2 producing and Th2, IL-4 producing responses.
- One of the immunologically discordant progressors became symptomatic during the course of the study, and he had a rapid drop in proliferative response to all antigens and also a shift from a Th1 to a Th2 response. To find out if the CD8 response also shifted in cytokine production, the CD8+ T-cell response to SLYNTVATL in this patient was also tested. It too was found to shift, from IFNgamma to IL-4 producing in Elispot, and using a bioassay of indicator lines, from IL-2 to IL-4 production.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Donor MHC A*0201, A11, B51, B61, Cw2, Cw14
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- Only 1/10 HLA A*02 carrying individuals in this study recognized SLYNTVATL.
- All HIV-1 proteins except Vpu were recognized, and responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location p17 (77–85)
Author Location
Epitope SLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Assay type cytokine production, proliferation, Tetramer binding, Intracellular cytokine staining, Chromium-release assay
References Dagarag *et al.* 2003

- Telomer length is short in the CD8+ T-cell compartment of HIV-1 infected people, indicating excessive CTL activation and premature senescense. Here human telomerase RT (hTERT) transduction of HIV-1-specific CTL was used to study the functional impact of telomerase. Telomerase expression enhanced proliferative capacity, as well as cytolytic and antiviral capabilities; cytokine production was unchanged. hTERT transduced

CTLs were 10-fold more efficient in controlling HIV-1 replication in culture. Thus telomerase transduction can restore CTL mediated cytolysis, and may have therapeutic potential.
- Three polyclonal CD8+ T-cell lines derived from an HIV-1, HLA A*0201 positive patient were used in this study, including one specific for this epitope.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Subtype B
Immunogen Vaccine
Vector/Type: peptide *HIV component:* p24 Gag
Species (MHC) mouse (A*0201)
Donor MHC A2.1
Assay type cytokine production, Chromium-release assay
Keywords binding affinity, vaccine-induced epitopes
References Okazaki *et al.* 2003

- Alanine substitutions of VIYQYMDDL were tested for importance of each amino acid for HLA-A2.1 binding. Peptide variant (vLyqymddV) showed an 8 fold higher MHC binding affinity than wild type. YLyqymddV had an even higher binding affinity, but the Y at position one blocked TCR recognition. The higher affinity form of vLyqymddV induced CTL *in vivo* that could protect against a vaccinia virus expressing RT and the wild type epitope.
- SLYNTVATL was included as a control.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Assay type Tetramer binding
Keywords genital and mucosal immunity
References Shacklett *et al.* 2003

- Lymphocytes from rectal biopsies were used to characterize the CD8+ T cell response to HIV in GALT, Gut-associated lymphoid tissues. Patients were selected on the basis of being HLA-A2+ and having detectable SLYNTVATL and ILKEPVHGV tetramer responses in PBMC. SLYNTVATL frequency was increased in GALT relative to PBMC in 6/7 patients studied, while a control response to a CMV-peptide was diminished in GALT. Only two patients had ILKEPVHGV CD8+ T cell responses, and both had slightly higher frequencies in GALT than PBMC.
- HIV may perturb lymphocyte retention in GALT, suggested by an overall reduction of GALT CD8+ cells expressing alphaE-beta7. GALT HIV-specific CD8+ T cells expressed alphaE-beta7, suggesting mucosal priming.

HXB2 Location p17 (77–85)
Author Location
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Tetramer binding, T-cell Elispot, Intracellular cytokine staining, Flow cytometric CTL assay
Keywords epitope processing, escape, variant cross-recognition or cross-neutralization
References Jamieson *et al.* 2003

- Epitope escape mutations in chronically infected individuals developed over several years indicating selective advantage of escape mutants. The maturation state of CTLs appear to affect the rate of epitope mutation and CTL decay.
- In two patients, SL9-specific CTL peaked at 2-4 years post-infection; at that point the escape mutations began to dominate followed by CTL decline with a 6 month lag, suggesting CTL decline resulted as a consequence of escape. In a third patient, the initial response was 1/2 as strong and mutations did not arise until 6-7 years post-infection; in that case the decline in SL9 CTL preceded epitope mutation.
- Two patients HLA-A*0201 started out with a non-consensus sequence, slFntvatl. In one of the patients, a transient reversion to the consensus was observed after 4 years, that did not reappear until the 11th year, suggesting the possibility that a reversion to the consensus form occurred, but a CTL response may have limited it so that this more fit form could not re-assert itself until the patient had a more severely compromised immune response.

HXB2 Location p17 (77–85)
Author Location Gag
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Country United States.
Assay type cytokine production, Tetramer binding, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords epitope processing, rate of progression, immunodominance, acute infection, dendritic cells, TCR usage, memory cells
References Kan-Mitchell *et al.* 2004

- SL9-specific CTLs were shown to be primed by immature DCs and independent of help from CD4+ or exogenous IL2, and sensitive to paracrine IL-2 induced apoptosis. The authors suggest that the reason SL9 responses are not seen during acute infection is the high level of innate immune responses resulting in cytokine-induced apoptosis, but that these CD8+ T-cells would come to dominate later infection when CD4 help is diminished.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Donor MHC A0201/2402, B52/75, Cw3; A0201/31, B27/5101, Cw2; A0207/2402, B46/52, Cw1
Country Japan.
Assay type Chromium-release assay

Keywords epitope processing, escape
References Yokomaku *et al.* 2004

- Epitope variants escaped from being killed by CTLs in an endogenous expression system although they were recognized when corresponding synthetic peptides were exogenously loaded onto the cells. Escape is thus probably due to changes that occur during the processing and the presentation of epitopes in infected cells.
- Endogenously expressed wild type epitope and slyntIatl variants were recognized by CTL clones while slynLvatl, slFntvaVl and sVyntvatl variants were not. sVyntvatl and slFntvaVl variants were, however, recognized when added exogenously to the cells.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost, vaccinia prime DNA boost *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease *Adjuvant:* GM-CSF
Species (MHC) human (A*0201)
Assay type cytokine production, CD8 T-cell Elispot - IFNγ, Tetramer binding, Chromium-release assay, Flow cytometric CTL assay
Keywords vaccine-specific epitope characteristics, immunodominance, characterizing CD8+ T cell responses
References Ferrari *et al.* 2004

- Thirteen HLA-A*0201 vaccines with anti-Gag CD8+ CTL reactivities were tested in uninfected HIV vaccine recipients to examine the pattern of SL9 epitope immunodominance. None of the vaccines had a detectable anti-SL9 response, in contrast to 75% of HLA A*0201 chronically infected HIV+ individuals that respond to this epitope.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords review, rate of progression, escape, acute infection
References Goulder & Watkins 2004

- This paper is a review of the role of CTL in HIV infection, and it uses SL9 as an example of an epitope that is not responded to early in infection, yet 75% of HIV+ people respond to SL9 during chronic infection. Despite the delay in response, strong SL9 responses have been associated with lower viral loads, and escape mutations arise.

HXB2 Location p17 (77–85)
Author Location (C consensus)
Epitope SLYNTVATL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen
Species (MHC) human (A*0202)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes that this epitope can be presented by A*0201 and A*0202.

HXB2 Location p17 (77–85)
Author Location p17 (SF2)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A*0202)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)
Epitope SLYNTVATL
Subtype B
Immunogen
Species (MHC) human (A*0205)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes that this epitope can be presented by A*0201 and A*0202.

HXB2 Location p17 (77–85)
Author Location p17 (subtype A)
Epitope SLYNTVATL
Subtype A
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A*0214, A*0201)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.
- The epitope variants SLYNTVATL and SLFNTVATL were both recognized.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Immunogen Vaccine
Vector/Type: vaccinia
Species (MHC) human (A2)
References Woodberry *et al.* 1999

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice.
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL).
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- SLYNTVATL was recognized by 5/16 HLA-A2 patients.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen Vaccine
Vector/Type: canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease
Species (MHC) human (A2)
Keywords immunodominance
References Carruth *et al.* 1999

- The vaccine used was a live recombinant canarypox (CP) virus vaccine containing multiple HIV-1 genes (HIV-1 MN gp120, HIV-1 LAI gp41, HIV-1 LAI Gag, HIV-1 LAI protease).
- CD4+ and CD8+ Gag and Env specific CTL responses were detected in only 1/5 vaccinated volunteers, and were not detectable 1 year after vaccination.
- CTL responses to epitopes SLYNTVATL and TVYYGVPVWK from HIV+ control patients were used as positive controls.
- The study explored why vaccinees were non-responsive – non-response was not due to inherent defects or differences in the ability of these individuals to process and present antigen.
- Lack of response to SLYNTVATL led the authors to speculate that the immunodominance of this epitope in natural infections may not be recapitulated by vaccine antigen.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Birk *et al.* 1998b

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Callan *et al.* 1998

- Included as a negative control in a tetramer study of A2-EBV CTL response.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Wagner *et al.* 1998a

- CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 HXB2)
Epitope SLYNTVATL
Epitope name SL9
Subtype B

Immunogen HIV-1 infection
Species (MHC) human (A2)
References Collins *et al.* 1998

- Two CTL clones recognize this epitope, but not the NL4-3 form of the epitope SLYNTIAVL.
- Nef down-regulates MHC class I molecules, which inhibits CTL killing, and this down-regulation can be partially compensated for by adding excess soluble peptide.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Durali *et al.* 1998

- Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia.
- Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested.
- Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag.
- Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef.
- Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env.
- Patient B18 had the greatest breadth and diversity of response, and recognized Gag SLYNTVATL and Nef PLTFGWCFKL.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords dendritic cells
References Kundu *et al.* 1998b

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients.
- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated.
- SLYNTVATL is a conserved HLA-A2 epitope included in this study – 3/6 patients had this sequence as their HIV direct sequence, one had the form SLYNTVAVL and all four of these had a detectable CTL response – the other two had either the sequence SLFSAVAVL or SLFSAVAAL and no detectable CTL response.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 IIIB)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.
- SLYNTVAVL, a variant found in HIV-1 MANC, was also recognized.
- SLFNTVAVL, a variant found in HIV-1 NY5CG, was also recognized.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A subtype consensus is SLfNtvatL.
- The D subtype consensus is SLyNTvATL.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords binding affinity
References Sewell *et al.* 1997

- Naturally occurring variants of this epitope escaped killing and acted as antagonists.
- The following variants were found in HIV-1 infected patients who mounted a strong response against this epitope: –F——, –F—-V-, –S——, -SF——, –L——, ——I—, ——I-V-, –F–I—, –F–I-V-, –F-A—-
- All variants bound to A2 with at least half the affinity of SLYNTVATL except the triple mutant: –F–I-V-
- Antagonism could be observed at low concentrations, abrogating lysis at an antagonist:agonist ratio of 1:10 – the antagonism was observed in one SLYNTVATL-specific CTL line but not another.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 HXB2)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords kinetics
References Yang *et al.* 1997b

- A chimeric universal T cell receptor was created by linking CD4 or an HIV-specific anti-gp41 Ig sequence to the signaling domain of the T cell receptor chain ζ, and transduced into CD8+ cells.
- The response using universal-receptor-bearing CD8+ cells to lyse infected cells *in vitro* was comparable to the natural occurring responses of CTL-clones from HIV+ individuals in terms of kinetics and efficiency.
- A CTL clone specific for this epitope was used for the comparison.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
References Stuhler & Schlossman 1997
- Keyhole limpit hemocyanin or tetanus toxoid Th epitope co-expression with peptide CTL epitopes on the same APC was required for induction of peptide-specific CTL.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Yang *et al.* 1996
- CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL.
- Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones.
- The distinction was thought to be due to lower expression of RT relative to Env and Gag.
- CTL can lyse infected cells early after infection, possibly prior to viral production.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CTL suppression of replication
References Yang *et al.* 1997a
- CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*.
- CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation.
- CTL suppress HIV replication more efficiently in HLA-matched cells.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Parker *et al.* 1992; Parker *et al.* 1994
- Examined in the context of motifs important for HLA-A2 binding.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords review
References McMichael & Walker 1994
- Review of HIV CTL epitopes.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Tsomides *et al.* 1994
- CTL clones recognize naturally processed peptide.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
References Stuhler & Schlossman 1997
- A three cell-type cluster consisting of APCs, Th, and CTLs is the minimal regulatory unit required for Th cell-dependent induction of CTLs.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Cao *et al.* 1997a
- The consensus peptides of B and D clade viruses and some Cs have the sequence SLYNTVATL.
- The consensus peptide of A, and some C strains have SLFNTVATL, a form that is cross-reactive.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dyer *et al.* 1999
- CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective.

- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords escape
References Harrer *et al.* 1998

- Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and -A2 (SLYNTVATL)
- Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 SF2)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords acute infection
References Altfeld *et al.* 2001a

- The relative contribution of CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection.
- Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells.
- The A2 epitopes Vpr AIIRLLQQL and p17 SLYNTVATL do not account for the dominance of Vpr and p17, the result holds even when HLA-A2+ individuals are excluded.

HXB2 Location p17 (77–85)
Author Location p17 (BRU)
Epitope SLYNTVATL
Epitope name SL9
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
Keywords epitope processing, dendritic cells
References Buseyne *et al.* 2001

- Exogenous presentation or cross-presentation of epitopes by antigen presenting cells (APC) without protein synthesis is an alternative pathway for CTL epitope processing that may be important in the initial generation of viral specific CTL.
- Dendritic cells treated with AZT to inhibit protein synthesis were able to elicit a strong specific CTL response in SLYNTVATL specific CTL line EM71-1 without protein synthesis, while macrophages demonstrated a decreased presentation efficiency.
- Exogenous Gag epitope presentation was Env-dependent and required receptor-dependent fusion.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Kostense *et al.* 2001

- HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load.
- Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional.
- In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival.
- In one patient with a SLYNTVATL response, no SLYNTVATL mutations were found among 21 clones despite high viral load (260,000 RNA copies/ml serum), suggesting low *in vivo* efficacy of the SLYNTVATL response.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, immunodominance
References Seth *et al.* 2001

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.
- 6/10 A*0201+ individuals had HIV-specific tetramer staining cells, and 5 of these declined upon successful therapy.
- 4/10 A*0201+ individuals with chronic HIV-1 infection recognized this epitope.
- Prior to therapy, the mean percentage of CD8+ cells that recognized the immunodominant epitope SLYNTVATL was six-fold greater than the percentage recognizing the epitope ILKEPVHGV.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, TCR usage
References Islam *et al.* 2001

- Transcript frequencies were followed for four CTL clones from patient 115, with a chronic and stable HIV-1 infection, and tracked in a longitudinal study of samples collected 6-11 years post infection: clone M21 and E15 recognize ERYLKDQQL, and clone D87 recognizes variant ERYLQDQQL, and clone p175b recognizes the A2 epitope SLYNTVATL.
- This epitope sequence from clone p175b uses the Vβ5, CDR3 (FDS), Jβ2.7 TCR beta gene.
- Responses were stable even through HAART with undetectable viral loads, but frequencies varied over time by 100-fold, ranging from 0.012% of the total population for SLYNTVATL at its lowest point to 3.78% for M21, with the relative frequencies of clones shifting over time.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 SF2)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 2/6 group 2, and 2/4 group 3.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLFNTVATL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A2)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- Variants SL(F/Y)NTVATL are A/B clade specific.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-A2 women, 1/10 HEPS and 22/26 HIV-1 infected women recognized this epitope, likelihood ratio 18.3, p value < 0.003, and ILK(D/E)PVHGV tended to be more reactive in HEPS women, SL(F/Y)NTVATL in infected women.
- The dominant response to this HLA allele was to this epitope in the 1/10 HEPS case and in 18 of the 22/26 HIV-1 infected women that responded.
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.
- Subject ML 1250 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, which switched to SL(F/Y)NTVATL post-seroconversion.
- Subjects ML 1575 and ML 1592 had no response to SL(F/Y)NTVATL prior to seroconversion, but made responses post-seroconversion.
- Subject ML 1760 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, and gained responses to epitopes A2 SL(F/Y)NTVATL and B27 KRWII(L/M)GLNK post-seroconversion.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 93TH253 subtype CRF01)
Epitope SLYNTIATL
Epitope name G77-85
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV positive controls, and 0/9 HIV negative women that were not exposed.
- This epitope was reactive in HIV+ control study subjects 125 and 144 who carried HLA-A2.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 93TH253 subtype CRF01)
Epitope SLYNTIATL
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 2/4 tested FSWs recognized the E clade version of this epitope, SLYNTIATL, the B clade version is SLYNTVATL.

- This epitope was only conserved in CRF01 and subtypes B and D, and exact matches were uncommon.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- SLYNTVATL was the dominant A2 epitope recognized in patients with chronic infection, except for Subject 11841 who recognized 5/8 epitopes.
- Three subjects had an A2 response only to SLYNTVATL.
- The two subjects with acute infection did not respond to SLYNTVATL.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords mother-to-infant transmission, escape
References Goulder *et al.* 2001c

- Immune escape variants in this epitope where transmitted both horizontally and vertically in two families.
- Eight transmitting mothers and 14 non-transmitting mothers were studied and variation within the SL9 epitope was associated carrying HLA-A2 (P=0.04), but no link between variation from the SL9 consensus and vertical transmission was established.

HXB2 Location p17 (77–85)
Author Location p17 (SF2)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.
- The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.

HXB2 Location p17 (77–85)
Author Location
Epitope SLYNTVATL
Epitope name Gag-SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A02, 17/30 (57%) recognized this epitope.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)
Epitope SLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, epitope processing, immunodominance
References Kelleher *et al.* 2001a

- Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in an intracellular context.
- RTV did not reduce antigen presentation and concentration of the two immunodominant Gag CTL epitopes (KRWIIMGLNK (B27) and SLYNTVATL (A2)).
- RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002

- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.
- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 NL43)
Epitope SLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords class I down-regulation by Nef
References Yang *et al.* 2002

- Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed *in vitro* than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL

susceptibility of NL-43. The CTL clone 18030D23, specific for the class I A2 presented SLYNTVATL epitope, was one of four used in this study.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 BRU)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords epitope processing
References Cohen *et al.* 2002

- The antigen presentation of two A2-restricted epitopes was compared, SLYNTVATL (p17) and ILKEPVHGV (RT). HIV-1 infected cells were more sensitive to lysis by SLYNTVATL-specific CTL than by ILKEPVHGV-specific CTL, because of a higher density of SLYNTVATL-A2 resulting from differences in processing.
- Incubation with a T1-cell proteolytic extract showed that by four hours, 25% of a p17 peptide had a C-term Leu-85 and were SLYNTVATL-precursors, while ILKEPVHGV-precursors were far less frequent (6.8%) even with four times more proteolytic extract after 30 hours.
- p17 was preferentially cleaved between Leu85 and Tyr86, while appropriate Val484 and Tyr485 cleavage was minor for RT.
- In a competition experiment, RSLYNTVATL bound TAP 3.7-fold more efficiently than RT peptides.
- No difference in CTL avidity was detected in six patients with HLA-A2-restricted responses to these epitopes.
- No significant difference in HLA-A2 binding to p17 or RT epitopes was observed.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* Gag, Pol *Adjuvant:* IL-12
Species (MHC) mouse (A2)
References Kmieciak *et al.* 2001

- Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with either a p17-p24-p51 fusion protein (vG/P-92) or the Gag-Pol precursor protein (vVK1).
- Compared to vVK1, vG/P-92 induced a significant increase in Gag and Pol induced IFNgamma production and CTL responses, and to the epitopes SLYNTVATL and ILKEPVHGV, as determined by Elispot and 51Cr-release assays.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A2, A3, B7, Bw6
Keywords HAART, ART
References Appay *et al.* 2002

- Four HIV patients with prolonged clinically successful antiviral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 NL-43)
Epitope SLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords class I down-regulation by Nef, escape
References Ali *et al.* 2003

- NL43 was passaged in the presence of Nef KEKGGLEGL-specific CTL clones STD11 and KM3, giving rise to rapid selection of escape mutations, including E93G, E93K, K94N+G99R, G95R+G99R, E98K, E98D, G99R, G99E, L100P, and L100I; insertions, deletions, frameshifts and an early stop codon. 34/36 (94%) of sequences carried mutations in the epitope by seven days, 36/36 (100%) by 14 days.
- Several mutations selected by KEKGGLEGL-specific CTL were shown to impair the down regulation of class I MHC by Nef, in particular E93G, E93K, and a truncation mutation at position 51.
- Nef deletion mutants increased 100-fold NL-43 susceptibility to inhibition by CTL specific for epitopes in other proteins, the A2 epitopes ILKEPVHGV in RT and SLYNTVATL in p17 Gag.

HXB2 Location p17 (77–85)
Author Location Gag
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Chromium-release assay, Flow cytometric CTL assay
Keywords class I down-regulation by Nef
References Bobbitt *et al.* 2003

- Nef, through Nef-mediated MHC-1 down-regulation, is not the only viral protein to influence levels of HIV-specific CTL recognition. The Rev L60F mutation, a common natural variant, can decrease CTL recognition of late gene products. The Rev mutation impacts the early to late gene switch, reducing late gene product production (Gag, Pol, Env, Vpu, Vpr and Vif), while increasing Nef production, both of which reduce the impact CTL recognition of late gene products. As expected, Rev L60F rendered HIV infected cells more resistant to CTL that recognized epitopes from the late proteins Env and Gag. Gag expression is reduced more than Env, and Gag-specific CTL were more profoundly affected. Conversely CTL against an epitope in an early gene product, Tat, were more effeciently recognized when infected with viruses carrying the Rev L60F mutation.
- Patients in the asymptomic phase with active immune responses had more CTL resistant viruses, with lower Rev activity, lower Gag expression and greater resistance to Gag-specific CTL killing, while viruses isolated from people with AIDS were more sensitive to CTL killing.

HXB2 Location p17 (77–85)
Author Location Gag (77–)
Epitope SLYNTVATL
Epitope name Gag77
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This epitope was one of the previously identified HLA-A2 epitopes studied.
- 10/17 HIV-infected HLA-A2+ people in this study recognized this epitope, and CTL and CD8+ T cells responses were elicted by immunization of transgenic mice with this peptide.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Intracellular cytokine staining
Keywords immunodominance, genital and mucosal immunity
References Kaul *et al.* 2003

- Predefined immunodominant peptide responses were used to compare CD8+ T-cell responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T-cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher.
- The immunodominant response was to this epitope in the PBMC of 1/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A2, A24, B38, B60, Cw2, Cw12
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), early treatment
References Montefiori *et al.* 2003

- HIV-1 + patient AC10 underwent early HAART treatment, which was discontinued 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTAVTL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Tetramer binding, Flow cytometric CTL assay
Keywords responses in children
References Sandberg *et al.* 2003

- 65 vertically HIV-1 infected children, ages 1-16, the majority undergoing ART, were analyzed in regard to their plasma viremia and CD4+ and CD8+ T-cell counts, and CD8+ T-cell responses.
- Using vaccina expressed Gag, Pol, Env, Rev, Nef in target cells in an Elispot assay, 85% of the children recognized at least one HIV antigen. Strong CD8+ T-cell responses were directed against Pol, followed by Gag and Nef. Children younger than 4 had significantly weaker responses (7/14 had no reponse) than older children (only 1/32 had no response, and responses were greater in magnitude).
- SLYNTVATL and ILKEPVHGV tetramers were used to quantitate specific responses. 49 chlidren in an expanded cohort carried HLA-A2. 1/11 children under 3 years of age had detectable CD8+ T-cell responses to SLYNTVATL, 2/11 to ILKEPVHGV. Among children over 3, 11/38 recognized SLYNTVATL and 9/38 recognized ILKEPVHGV.
- Older children that maintained a CD4 count greater than 400 cells/ul tended to have stronger CTL reponses.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) (A2)
Donor MHC A2, A3, B27, B51; A2, A3, B27, B57; A2, A23, B57
Assay type cytokine production, CD8 T-cell Elispot - IFNγ, Tetramer binding, Intracellular cytokine staining
Keywords assay standardization/improvement, memory cells
References Sun *et al.* 2003

- This study compares assay methods for testing CTL responses using samples from 20 HIV+ patients. The study compares ELISpot, tetramer-binding, and intracellular IFNγ. Tetramer-bidning analysis was performed with Gag (SLYNTVATL) or Pol (ILKEPVHGV) tetramers. Antigen presentation using recombinant vaccinia viruses (rVVs) encoding HIV-LAI Gag,

Pol, Env, Nef, Tat and Vif proteins was compared to peptide panels. HIV antigen recognition in memory CTLs was measured by chromium release assay and compared to effector/memory CD8+ T-cells in an IFN-γ ELISpot assay.
- Results: IFNγ Elispot and flow cytometry gave similar frequencies of HIV specific CD8+ T-cells. Tetramer-binding analysis was most sensitive. Pools of peptides and the sum of frequencies of individual peptides were comparable. Elispot assays using peptides were more sensitive than assays using vaccinia expressed proteins. Cr release and Elispot against rVVs gave comparable memory cell responses 2/3s of the time.
- 3/7 HLA-A2+ patients recognized this epitope.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 NL43)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Chromium-release assay, CTL suppression of replication
Keywords escape, TCR usage
References Yang *et al.* 2003a

- Virus was cultured in the presence of CTL lines specific for 5 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, SEGATPQDL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts.
- Three CTL clones were studied that recognized SLYNTVATL, 161JxA14, 18030D23, and 115DEC4. The different TCR usage on the CTL clones resulted in different patterns of recognition and escape. 161JxA14 suppressed the variant slFntvatl, 18030D23 did not; conversely the variants slfntIaVl and slFntIatl were suppressed by 18030D23, but not 161JxA14.
- After two weeks of passage the predominant escape mutant from 161JxA14 was slyntIatl. Amino acid residues flanking SL9 were unchanged. Escape mutations did not occur within two weeks for the two additional SL9-specific CTL clones 18030D23 and 115DEC4.

HXB2 Location p17 (77–85)
Author Location p17 (43)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
Assay type CTL suppression of replication
Keywords class I down-regulation by Nef, early-expressed proteins, kinetics
References Ali *et al.* 2004

- Translocation of the gag SLYNTVATL epitope into the early expressed Nef protein resulted in increased antiviral efficiency of SL9 specific CTLs in culture and the loss of MHC-I down-regulation by Nef, indicating that both the timing of epitope expression and reduction of MHC-I affect the ability of CTLs to supress HIV-1.

HXB2 Location p17 (77–85)
Author Location Gag (77–85 B con)
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords variant cross-recognition or cross-neutralization
References Draenert *et al.* 2004c

- CD8+ T-cell responses that persisted in individuals with advanced disease were studied; most of the optimal epitopes defined were recognized with intermediate to high avidity. On average 13 (range, 2-39) epitopic regons were targeted in an average of 6 proteins (range, 1-8). HAART resulted in decrease in antigen and reduction in gamma IFN EliSpot responses, suggesting active responses to autologous virus. Limited or no mutations within most viral epitopes suggest that persistent CTL through late disease do not exert strong immune selection pressure, yet the Elispot assays show robust responses, suggesting to the authors that gamma IFN based screening methods may not reveal functional CD8+ T-cell impairment in patients with AIDS.
- Three subjects recognized this epitope, with high functional avidity. Relative to consensus, two individuals that had the SLYNTVATL epitope carried a R -> K mutation proximal to but outside the epitope; possible processing implications were not studied here.

HXB2 Location p17 (77–85)
Author Location Gag
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 patients showed reduced in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- 2/11 HLA A2+ infection-resistant men, compared to 7/9 men pre-seroconversion who went on to become infected, reacted to this epitope.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)

Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 14/19 patients recognized this epitope, it was the most commonly recognized of 9 HLA A*02 epitopes tested.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Epitope name SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Chromium-release assay
Keywords binding affinity, TCR usage, characterizing CD8+ T cell responses
References Yang *et al.* 2003b

- Killing efficiency of CTLs and their ability to suppress viral replication is shown to depend more on epitope specificity than to antigenic avidity. Different clones recognizing the same epitope had similar killing efficiency despite their variation in avidity. Nef specific CTL clones tended to be most inhibitory, followed by Gag, then by RT specific clones, regardless of avidity.
- 3/14 CTL T-cell clones tested were specific for Gag/p17-SL9. Under conditions of excess peptide (100ug/ml), there was no difference in their lytic potential; all possessed similar effector capacity. Avidity was measured as the sensitizing dose of peptide required for 50% of maximal killing (SD50), which varied from 20 pg/ml to 100 ng/ml, over four orders of magnitude for all 14 epitopes. The SD50 range for Gag/p17-SL9 was 1,000 - 20,000 pg/ml.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type cytokine production, proliferation, CD8 T-cell Elispot - IFNγ, Tetramer binding, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Flow cytometric CTL assay
Keywords HAART, ART, memory cells, characterizing CD8+ T cell responses
References Daniel *et al.* 2004

- CD4+ and CD8+ responses in chronically HIV-1 infected patients on HAART were weak with decreased polyclonality. Only 33% of patients had CD4+ T-cells that could proliferate, and only 22% had HIV-specific CD8+ T-cell responses, and those rare responses showed low perforin levels and persistent expression of CD27, indicating incomplete differentiation and loss of lytic function.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country United States.
Assay type proliferation, Tetramer binding, T-cell Elispot
Keywords acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Lichterfeld *et al.* 2004a

- HIV-1 specific CD8+ T-cells in acute and long-term nonprogressive HIV-1 infection show strong ex-vivo proliferative capacities which are rapidly lost in chronic HIV-1 infection. The loss of CD8+ T-cell function is closely linked with the loss of HIV-1 specific, IL2 secreting CD4+ T-cells. The function can be rescued in vitro and in vivo by restoring the specific CD4+ T-cell help.
- Despite being detectable at high frequencies, CD8+ T-cells specific for SL9 epitope were shown to entirely lose their proliferative capacity in chronic HIV-1 infection. This activity could be restored by co-stimulation with CD4+ T cells isolated from acute infection in an IL-2 dependent manner.

HXB2 Location p17 (77–85)
Author Location Gag (77–85)
Epitope SLYNTVATL
Epitope name gag 77-85
Subtype B
Immunogen HIV-1 infection, HIV-2 infection
Species (MHC) human (A2)
Country Gambia.
Assay type Tetramer binding, Intracellular cytokine staining
Keywords escape, TCR usage, variant cross-recognition or cross-neutralization, characterizing CD8+ T cell responses
References Lopes *et al.* 2003

- CD8+ T cells from HIV-2 infected patients had more polyclonal TCR responses than HIV-1 infected patients, who tended to have oligoclonal responses. This results in limited plasticity of T cell responses to amino acid substitutions within epitopes in HIV-1 infections. HIV-2-specific CD8+ T-cells showed a more diverse TCR usage associated with enhanced CD8 expansion and IFN-gamma production on cross-recognition of variant epitopes.
- Responses to this epitope were characterized in detail. One patient's response to SL9 A2-SLYNTVATL tetramers was shown to have only Vbeta5.1 clonotypes. The naturally occuring HIV-2 variant: slFntvCVI, was not recognized well by this response or by the SLYNTVATL reactive CD8+ T cells in four additional A2+ HIV infected asymptomatic individuals. The subtype A variant, slFntvatl was also poorly recognized, and 4/5 Ala substitutions abrogated responses. All variants bound to HLA-A2 with higher affinity than the index peptide except slyntAatl, which was slightly reduced, so the lack of cross-reactivity must have been due to the TCR.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLYNTVATL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Chromium-release assay
Keywords assay standardization/improvement
References Lubong *et al.* 2004

- Using IL7 or IL15 in culturing of HIV-1 specific CTL clones was inferior to using IL-2 alone and the addition of these cytokines to IL-2 did not show any advantage. Neither proliferation, survival or lytic capacity of HIV-1-specific CTLs was significantly enhanced by addition of IL7 or IL15.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2)
Donor MHC A02, A30, B4402, B15
Assay type Tetramer binding, T-cell Elispot
Keywords HIV exposed persistently seronegative (HEPS)
References Missale *et al.* 2004

- HIV-specific T-cell response was tested in HIV-uninfected patients exposed to blood from a patient with highly replicating HIV; these same patients were nosocomially infected with HBV. HIV-specific T-cell responses were directed to structural and non-structural HIV proteins in two patients suggesting that the virus replicated in these patients sufficiently to prime a cell-mediated immune response that protected these individuals from HIV infection.
- This patient responded to 4/8 HIV epitopes tested in an IFNgamma EliSpot assay or tetramer assay. Responses were detected 8 and 28 weeks after exposure. No response to SLYNTVATL was detected by either assay.

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country United Kingdom.
Assay type Tetramer binding, T-cell Elispot, Intracellular cytokine staining
Keywords rate of progression, acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Papagno *et al.* 2004

- Acute HIV-1 infection induces massive activation of HIV-specific and non-HIV-specific CD8+ T-cells resulting in differentiation of these cells. High differentiation of CD8+ T-cells is correlated with disease progression. Differentiation is a natural process but it can be driven by elevated immune activation, such as in HIV infection.

HXB2 Location p17 (77–85)
Author Location p17 (77–85)
Epitope SLFNTVATL
Epitope name SLF
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, Tetramer binding, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, immunodominance, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses, and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This epitope was one of six epitopes found to be under positive selection for escape mutations and was completely replaced by escape variants between days 327 and 635 (slYntvatl and slYnAvatl).

HXB2 Location p17 (77–85)
Author Location p17
Epitope SLYNTVATL
Epitope name SL9
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2, A*0202)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among B and D clade viruses.
- The Clade A version of the epitope, SLFNTVATL, was preferentially recognized by CTL.
- This epitope was recognized by two different exposed seronegative prostitutes.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)
Epitope SLYNTVATL
Epitope name LR23
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG
Species (MHC) mouse (A2.1)

Keywords binding affinity, vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2001

- The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01).
- The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.
- HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants.
- All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.

HXB2 Location p17 (77–85)
Author Location p17 (77–85 LAI)
Epitope SLYNTVATL
Epitope name LR23
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30
Species (MHC) mouse (A2.1)
Keywords vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2002

- When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination Peter *et al.* [2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.

HXB2 Location p17 (77–86)
Author Location Gag
Epitope SLYNTVATLY
Epitope name 1261
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A01, A02, B08, ?, Cw16, ?; A02, A30, B35, B49, Cw04, Cw07; A02, A03, B7, B58, Cw07; A02, A03, B08, B51, Cw01, Cw07
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for SLYNTVATLY: 78%

HXB2 Location p17 (78–86)
Author Location p17
Epitope LYNTVATLY
Epitope name LY-9
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*2902, B*4403)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, epitope processing, immunodominance, cross-presentation by different HLA
References Masemola *et al.* 2004b

- Highly targeted regions in Gag for CD8+ T-cells were defined for individuals with C clade infections in South Africa. Nine specific epitopes within the most reactive regions were characterized. This is one of five novel epitopes that were found among subtype C HIV-1 from African patients that hadn't previously been identified in B clade infections. Some epitopes were shown to be promiscuous, presented by multiple class I restricting alleles.
- LYNTVATLY was presented by A*2902 and B*4403. B*44 is more common among Caucasians than Zulus (allele frequency 0.149 versus 0.107), while A*29 is more common in Zulus (0.045 versus 0.125).

HXB2 Location p17 (78–86)
Author Location (C consensus)
Epitope LYNTVATLY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A29)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p17 (80–88)
Author Location Gag (80–)
Epitope NTVATLYCV
Epitope name Gag80
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* p17 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was an intermediate A2 binder, and induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.

HXB2 Location p17 (82–91)
Author Location p17 (82–91 93TH253 subtype CRF01)
Epitope IATLWCVHQR
Epitope name G82-91
Subtype CRF01_AE
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11.
- This epitope was strongly reactive in HIV+ study subject 053 who carried HLA-A11.

HXB2 Location p17 (82–91)
Author Location p17 (82–91 93TH253 subtype CRF01)
Epitope IATLWCVHQR
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined.
- 3/8 tested FSWs recognized this epitope.
- This epitope was not conserved in other subtypes, and exact matches were uncommon.

HXB2 Location p17 (84–91)
Author Location Gag (83–90)
Epitope TLYCVHQR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords inter-clade comparisons, TCR usage
References Fukada *et al.* 2002

- Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals.
- TLYCVHQR was found to elicit clade-specific responses in clade B (TLYCVHQR is most common, and is also common in clade A – the variant tlycvhqK is common in clade B) and clade E (tlWcvhqr is most common). TLYCVHQR was not recognized by any CTL, tlycvhqK was recognized by CTL from 1/5 B clade infected Japanese subjects, and tlWcvhqr was not recognized by CTL from infected Thai subjects, so this seems to be a B clade exclusive epitope.
- The binding of the variant peptides to HLA A*1101 was comparable, but CTL that recognized tlycvhqK did not cross-recognize the other forms, implicating TCR interaction differences.

HXB2 Location p17 (84–91)
Author Location p17 (83–91)
Epitope TLYCVHQR
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords escape
References Harrer *et al.* 1998

- Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and HLA-A2 (SLYNTVATL)
- Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape.
- A Q90E substitution resulted in a loss of the ability of the peptide to induce lysis, a R91K substitution was still reactive, and a R91Q substitution showed a reduced ability to stimulate lysis.

HXB2 Location p17 (84–92)
Author Location p17 (84–92)
Epitope TLYCVHQRI
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes that this is an A*1101 epitope.

HXB2 Location p17 (84–92)
Author Location Gag (83–91 SUMA)
Epitope TLYCVHQKI
Epitope name Gag TI9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*1103)
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T-cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location p17 (84–92)
Author Location p17 (84–92)
Epitope TLYCVHQRI
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords responses in children, mother-to-infant transmission
References Brander & Walker 1995

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.

HXB2 Location p17 (84–92)
Author Location p17 (84–92)
Epitope TLYCVHQRI
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Birk *et al.* 1998b

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (84–92)
Author Location p17 (84–92)
Epitope TLYCVHQRI
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p17 (84–92)
Author Location p17 (84–92 SF2)
Epitope TLYCVHQRI
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 1/2 group 3.

HXB2 Location p17 (84–92)
Author Location p17 (84–92)
Epitope TLYCVHQRI
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location p17 (86–101)
Author Location p17 (SF2)
Epitope YCVHQRIEIKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.
- The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.

HXB2 Location p17 (86–101)
Author Location p17 (SF2)
Epitope YCVHQRIEIKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.
- The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.

HXB2 Location p17 (87–105)
Author Location p17 (91–105 SF2)
Epitope CRIDVKDTKEALEKIE
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location p17 (88–115)
Author Location p17 (88–115 ARV)
Epitope VHQRIEIKDTKEALDKIEEEQNKSKKKA
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Achour *et al.* 1990

- B cell epitope HGP-30 also serves as a CTL epitope.

HXB2 Location p17 (88–115)
Author Location p17 (88–115 ARV)
Epitope VHQRIEIKDTKEALDKIEEEQNKSKKKA
Immunogen Vaccine *Vector/Type:* peptide *HIV component:* CD4BS, HPG30, V3 *Adjuvant:* IL-12
Species (MHC) mouse (H-2^{d})
References Hamajima *et al.* 1997

- B cell epitope HGP-30 also serves as a CTL epitope.
- Vaccine combined HGP-30, V3 loop peptide variants, and CD4 binding site peptide.
- IL-12 expression plasmid included with the vaccination enhanced the CTL response.

HXB2 Location p17 (91–101)
Author Location p17 (SF2)
Epitope RIDVKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in an HIV+ Haitian living in Boston, who was A23/68 B45/72 Cw2/16 – this epitope fell outside the most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (91–105)
Author Location p17 (91–105 SF2)
Epitope RIDVKDTKEALEKIE
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A3, A24, B8, B55.

HXB2 Location p17 (92–101)
Author Location p17 (92–101)
Epitope IEIKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human (B*4001)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4001 epitope.

HXB2 Location p17 (92–101)
Author Location p17
Epitope IEIKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human (B60)
References Wagner *et al.* 1998a

- CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules.

HXB2 Location p17 (92–101)
Author Location p17 (92–101 SF2)
Epitope IEIKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human (B60)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.

- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 1/1 group 2, and 0/0 group 3.

HXB2 Location p17 (92–101)
Author Location Gag (92–101)
Epitope IEIKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human (B60)
Keywords class I down-regulation by Nef
References Yang *et al.* 2002

- Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed *in vitro* than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL43 infected cells. The CTL clone 161JD27, specific for the class I B60 presented epitope IEIKDTKEAL, was one of four used in this study.

HXB2 Location p17 (92–101)
Author Location p17 (92–101 NL43)
Epitope IEIKDTKEAL
Epitope name IL10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B60)
Assay type Chromium-release assay, CTL suppression of replication
Keywords escape
References Yang *et al.* 2003a

- Virus was cultured in the presence of CTL lines specific for 5 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, SEGATPQDL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts.
- There was one cloned cell line that recognized IEIKDTKEAL, 161JD27. After 2 weeks of passaging HIV-1 in the presence of 161JD27, no mutations were observed within the epitope in 10 sequences; one of the 10 had a single E -> K substitution 6 amino acids beyond the C-terminal end of the epitope.

HXB2 Location p17 (92–101)
Author Location Gag (92–101 B consensus)
Epitope IEIKDTKEAL
Epitope name IL10
Subtype B
Immunogen Vaccine
Vector/Type: adeno-associated virus (AAV)
HIV component: gp120
Species (MHC) human (B60)
Assay type Chromium-release assay, Flow cytometric CTL assay
Keywords dynamics, immune evasion
References Brainard *et al.* 2004

- HIV-1 gp120 is shown to suppress the ability of antigen-specific CTLs to migrate or remain at sites of high viral replication by concentration-dependent chemotaxis and fugetaxis. Directional T-cell movement is shown to depend on the interaction of the V2 and V3 loops with the CXCR4 receptor. X4 HIV-1 gp120 causes the migration of T-cells, including HIV-1 specific CTL, away from infected target cells, another potential mechanism for immune evasion.

HXB2 Location p17 (92–101)
Author Location p17 (92–101)
Epitope IEIKDTKEAL
Epitope name Gag/p17-IL10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B60)
Assay type Chromium-release assay
Keywords binding affinity, epitope processing, TCR usage, characterizing CD8+ T cell responses
References Yang *et al.* 2003b

- Killing efficiency of CTLs and their ability to suppress viral replication is shown to depend more on epitope specificity than to antigenic avidity. Different clones recognizing the same epitope had similar killing efficiency despite their variation in avidity. Nef specific CTL clones tended to be most inhibitory, followed by Gag, then by RT specific clones, regardless of avidity.
- 1/14 CTL T-cell clones tested were specific for Gag/p17-IL10. Under conditions of excess peptide (100ug/ml), there was no difference in their lytic potential; all possessed similar effector capacity. Avidity was measured as the sensitizing dose of peptide required for 50% of maximal killing (SD50), which varied from 20 pg/ml to 100 ng/ml, over four orders of magnitude for all 14 epitopes. The SD50 value for the Gag/p17-IL10 clone was 8,000 pg/ml.

HXB2 Location p17 (92–101)
Author Location p17 (SF2)
Epitope IEIKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human (B60, B*4001)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes.
- B60 is present in 10-20% of the Caucasoid and very common in Asian populations.

HXB2 Location p17 (92–101)
Author Location p17 (92–101)
Epitope IEIKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human (B60, B61)

Keywords immunodominance
References Day *et al.* 2001

- No immunodominant responses were detected to five B61-restricted epitopes tested.
- All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response.

HXB2 Location p17 (93–101)
Author Location p17 (SF2)
Epitope DVKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ Caucasian from Boston, who was A1/*0201 B8/63 Cw7/- – this epitope fell outside the most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p17 (93–101)
Author Location Gag (99–107 WEAU)
Epitope EVKDTKEAL
Epitope name Gag EVL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Donor MHC A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- There was a weak response to this epitope during acute and early infection, and the epitope sequence did not vary during the first year of the infection.

HXB2 Location p17 (93–101)
Author Location p17 (93–101)
Epitope EIKDTKEAL
Immunogen Peptide-HLA interaction
Species (MHC) human (B8)
References DiBrino *et al.* 1994b

- Examined in the context of motifs important for HLA-B8 binding, predicted epitope based on Achour *et al*.

HXB2 Location p17 (93–101)
Author Location p17 (93–101)
Epitope EIKDTKEAL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Birk *et al.* 1998b

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (93–101)
Author Location p17 (93–101 LAI)
Epitope EIKDTKEAL
Subtype B
Immunogen
Species (MHC) human (B8, B60)
References Brander & Walker 1997

- Pers. comm. from A. Trocha and S. Kalams to C. Brander and B. Walker.

HXB2 Location p17 (119–127)
Author Location Gag (119–127 BORI)
Epitope AADTGNSSQ
Epitope name Gag AQ9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*2902, B*1402, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, acute infection, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.

- The patient BORI had high viral loads and rapid CD4 decline. BORI mounted 8 detected responses. BORI did not control viral replication well, and escape mutations occurred early and in most epitopes, 6/7 that were precisely identified.
- 20 variants in the AADTGNSSQ epitope were found in the patient BORI, the first appearing at day 35 with new variants continuing to arise through day 556. This is an extremely variable epitope, and changed not only by base substitution but by insertion and deletion. All variants tested conferred escape, at high concetrations of peptide.

HXB2 Location p17 (121–132)
Author Location p17 (121–132 HXB2R)
Epitope DTGHSNQVSQNY
Immunogen HIV-1 infection
Species (MHC) human (A33)
References Buseyne *et al.* 1993b

- Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.

HXB2 Location p17 (121–132)
Author Location Gag (121–132 LAI)
Epitope DTGHSNQVSQNY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A33)
References Buseyne *et al.* 1993a

- Vertical transmission of HIV ranges from 13% to 39%.
- Primary assays showed that cytotoxic activity against at least one HIV protein was detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM17 (CDC P2A+C+D2) had a CTL response to two epitopes in Gag.

HXB2 Location p17 (124–132)
Author Location p17 (124–132 LAI)
Epitope NSSKVSQNY
Subtype B
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004

- Noted by Brander to be B*3501 epitope.

HXB2 Location p17 (124–132)
Author Location p17
Epitope NSSQVSQNY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords binding affinity
References Dorrell *et al.* 2001

- The crystal structure of this epitope bound to HLA-B*3501 shows that a serine can fit into the B pocket, which is shared between B35 and B53, with the hydroxyl group of the P2 serine occupying a position almost identical to the P2 proline that was previously considered the anchor motif.
- Novel B53 epitopes (DTINEEAAEW and QATQEVKNM) were defined in this study that showed that A and T can also serve as P2 anchor residues for the B pocket of HLA-B35 and B53 – while S, T, and P could all fit into the B pocket and form a hydrogen bond, A would not form a bond, so the authors propose compensatory interactions account for the high affinity of QATQEVKNM for B53.

HXB2 Location p17 (124–132)
Author Location p17 (124–132 LAI)
Epitope NSSKVSQNY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords review
References McMichael & Walker 1994

- Review of HIV CTL epitopes.

HXB2 Location p17 (124–132)
Author Location
Epitope NSSKVSQNY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords dynamics, acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location p17 (124–132)
Author Location p17 (124–132)
Epitope NSSKVSQNY
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Birk *et al.* 1998b

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.

HXB2 Location p17 (124–132)

Author Location p17 (124–132 LAI)
Epitope NSSKVSQNY
Subtype B
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human (B35)
References Rowland-Jones *et al.* 1995

- Established by titration.

HXB2 Location p17 (124–132)
Author Location p17 (124–132 LAI)
Epitope NSSKVSQNY
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (B35)
References Lalvani *et al.* 1997

- A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers.
- This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors.

HXB2 Location p17 (124–132)
Author Location p17
Epitope NSSKVSQNY
Immunogen
Species (MHC) human (B35)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive.
- HIV-2 version of this epitope is not conserved: PPSGKGGNY, but the CTLs are cross-reactive – this is one of five B35 CTL epitopes that are cross-reactive, see also Rowland-Jones *et al.* [1995].

HXB2 Location p17 (124–132)
Author Location p17
Epitope NSSKVSQNY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART
References Seth *et al.* 2001

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.

HXB2 Location p17 (124–132)
Author Location p17 (124–132 SF2)
Epitope NSSKVSQNY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3.

HXB2 Location p17 (124–132)
Author Location
Epitope NSSKVSQNY
Epitope name Gag-NY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B35, 1/21 (5%) recognized this epitope.

HXB2 Location p17 (124–132)
Author Location p17 (124–132)
Epitope NSSKVSQNY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2/9 patients recognized this epitope.

II-B-2 Gag p17-p24 CTL, CD8+, epitopes

HXB2 Location p17-p24 (124–1)
Author Location Gag (124–133 BORI)
Epitope NSSQVSQNYP
Epitope name Gag NP10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human

Donor MHC A*2902, B*1402, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, acute infection, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient BORI had high viral loads and rapid CD4 decline. BORI mounted 8 detected responses. BORI did not control viral replication well, and escape mutations occurred early and in most epitopes, 6/7 that were precisely identified.
- 10 variants in the NSSQVSQNYP epitope were found in the patient BORI, the first appearing at day 35, NgSQVSQNYP, with new variants continuing to arise through day 556. This is an extremely variable epitope, and changed not only by base substitution but by insertion and deletion. All variants tested conferred some degree of escape by diminishing the CTL response.

HXB2 Location p17-p24 (127–3)
Author Location p17-p24 (127–135 subtype D)
Epitope QVSQNYPIV
Subtype D
Immunogen
Species (MHC) human (A*6802)
References Dong 1998

- Epitope starts in p17 and ends in p24.
- Predicted on binding motif, no truncations analyzed.

HXB2 Location p17-p24 (131–6)
Author Location p17-p24 (132–140 SF2)
Epitope NYPIVQNL
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- The epitope starts in p17 and ends in p24.
- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 1/4 HIV-1 + people tested.
- NYPIVQNL bound to A*2402 with medium strength, and the epitope can be processed in a vaccinia construct and presented – no CTL clone was obtained.

II-B-3 Gag p24 CTL, CD8+, epitopes

HXB2 Location p24 (8–17)
Author Location p24 (140–149)
Epitope GQMVHQAISP
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others.

HXB2 Location p24 (8–20)
Author Location p24 (140–152 IIIB)
Epitope GQMVHQAISPRTL
Immunogen HIV-1 infection
Species (MHC) human (Cw3)
References Littaua *et al.* 1991

- Fine specificity of human Cw3 restricted Gag CTL epitope.

HXB2 Location p24 (8–20)
Author Location p24 (8–20)
Epitope GQMVHQAISPRTL
Immunogen HIV-1 infection
Species (MHC) human (Cw3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location p24 (8–27)
Author Location p24 (140–159)
Epitope GQMVHQAISPRTLNAWVKVV
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Musey *et al.* 1997

- CTL specific for this epitope were found in the peripheral blood but not in the cervical mucosa of one donor.

HXB2 Location p24 (9–18)
Author Location Gag (173–182)

Epitope QMVHQAISPR
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location p24 (10–18)
Author Location Gag (144–152 SF2)
Epitope MVHQAISPR
Subtype B
Immunogen HIV-1 infection, computer prediction
Species (MHC) human (A*3303)
Assay type Chromium-release assay
Keywords binding affinity, computational epitope prediction
References Hossain *et al.* 2003

- HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing.
- This epitope is one of the 4 that are properly processed.

HXB2 Location p24 (10–18)
Author Location Gag (174–182)
Epitope MVHQAISPR
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location p24 (11–20)
Author Location (C consensus)
Epitope VHQAISPRTL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1510)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (11–24)
Author Location p24 (SF2)
Epitope VQHAISPRTLNAWV
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in an HIV+ Haitian living in Boston, who was A34/68 B57/71 Cw3/7 – this epitope fell outside the most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p24 (11–25)
Author Location p24 (11–25 HXB2)
Epitope VHQAISPRTLNAWVK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started

treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 29% of the study subjects, and it was the third most frequently recognized peptide.

HXB2 Location p24 (11–32)
Author Location p24 (143–164 BH10)
Epitope VHQAISPRTLNAWVKVVEEKAF
Immunogen HIV-1 infection
Species (MHC) human (Bw57)
References Johnson *et al.* 1991
- Gag CTL response studied in three individuals.

HXB2 Location p24 (12–20)
Author Location Gag (146–154)
Epitope HQAISPRTL
Immunogen HIV-1 infection
Species (MHC) chimpanzee (Patr-B*02)
References Balla-Jhagjhoorsingh *et al.* 1999b
- Certain HLA-alleles have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57.
- Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS.
- CTL responses were studied in two HIV-1 infected chimpanzees that have strong CTL responses, and they were found to respond to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57.
- The human HLA protein which presents this Patr-B*02 epitope is HLA-B*5701 but the amino acid sequences in the binding pockets of HLA-B*5701 and Patr-B*02 are distinctive.

HXB2 Location p24 (13–20)
Author Location p24 (145–152)
Epitope QAISPRTL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (Cw3)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location p24 (13–23)
Author Location p24 (145–155)
Epitope QAISPRTLNAW
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Betts *et al.* 2000
- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to QAISPRTLNAW noted previously to be A25.

HXB2 Location p24 (13–23)
Author Location p24 (145–155 LAI)
Epitope QAISPRTLNAW
Subtype B
Immunogen
Species (MHC) human (A*2501)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes that this is an A*2501 epitope.

HXB2 Location p24 (13–23)
Author Location p24 (145–155 SF2)
Epitope QAISPRTLNAV
Immunogen HIV-1 infection
Species (MHC) human (A25)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b
- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with preseroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A25+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/2 group 2, and 1/3 group 3.

HXB2 Location p24 (13–23)
Author Location Gag (145–155 IIIB)
Epitope QAISPRTLNAW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A25)
Assay type Chromium-release assay
References Kurane *et al.* 2003
- Three CD8+ CTL cell clones were derived from 2 HIV-1 positive asymptomatic patients, and their epitope specificities and HLA presenting proteins were defined.

HXB2 Location p24 (13–23)
Author Location p24 (145–155 LAI)
Epitope QAISPRTLNAW
Subtype B
Immunogen
Species (MHC) human (A5)
References Kurane & West 1998

HXB2 Location p24 (15–23)
Author Location
Epitope LSPRTLNAW
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- ISPRTLNAW was consistently recognized by 1/22 HEPS sex worker controls (ML1250), and LSPRTLNAW was recognized by 2 additional HEPS sex worker controls (ML1693 and ML1589).

HXB2 Location p24 (15–23)
Author Location p24
Epitope LSPRTLNAW
Immunogen HIV-1 infection
Species (MHC) human (B*57)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002

- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.
- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location p24 (15–23)
Author Location p24 (147–155 IIIB)
Epitope ISPRTLNAW
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5701 epitope.

HXB2 Location p24 (15–23)
Author Location
Epitope ISPRTLNAW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords rate of progression, immunodominance
References Migueles & Connors 2001

- HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.

HXB2 Location p24 (15–23)
Author Location
Epitope ISPRTLNAW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords rate of progression, immunodominance
References Migueles & Connors 2001

- CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.
- CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia.
- The HLA-A*0201 SLYNTVATL epitope response was not as strong in individuals that carried both A2, B57.

HXB2 Location p24 (15–23)
Author Location
Epitope ISPRTLNAW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Assay type Intracellular cytokine staining, Flow cytometric CTL assay
Keywords rate of progression, escape
References Migueles *et al.* 2003

- cDNA Gag sequences from a set of 17 HLA-B*5701+ progressors and 10 LTNPs were obtained, and the variation in four p24 B*5701 epitopes examined. Sequence variants were more common ($p < 0.01$) in the epitopes in the progressors (median 3, range 1-7) than LTNPs (median 2, range 0-4).
- In general use of the autologous protein in a target cell did not diminish the overall CD8+ T-cell responses.

HXB2 Location p24 (15–23)
Author Location Gag (147–155 LAI)
Epitope ISPRTLNAW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701, B*5801)
Keywords rate of progression
References Klein *et al.* 1998

- B57 has been associated with long-term non-progression in the Amsterdam cohort.

- The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag.

HXB2 Location p24 (15–23)
Author Location p24 (147–155)
Epitope ISPRTLNAW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others, but not SLYNTVATL.

HXB2 Location p24 (15–23)
Author Location Gag (SF2)
Epitope ISPRTLNAW
Epitope name IW9
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords acute infection
References Goulder *et al.* 2001a

- This epitope elicited the second strongest CTL response in patient PI004 during acute infection, and maintained the response.
- Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.

HXB2 Location p24 (15–23)
Author Location p24 (147–155)
Epitope ISPRTLNAW
Epitope name ISP
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- None of the 8 study subjects recognized this epitope but none were HLA B57+.

HXB2 Location p24 (15–23)
Author Location p24 (15–23)
Epitope ISPRTLNAW
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (15–23)
Author Location p24 (147–155 SF2)
Epitope ISPRTLNAW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 2/2 group 3.

HXB2 Location p24 (15–23)
Author Location
Epitope ISPRTLNAW
Epitope name Gag-IW9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B57, 2/5 (40%) recognized this epitope.
- Among HIV+ individuals who carried HLA B58, 0/4 (0%) recognized this epitope.

HXB2 Location p24 (15–23)
Author Location
Epitope ISPRTLNAW
Epitope name ISP
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFN? Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location p24 (15–23)

Author Location Gag (147–155)
Epitope ISPRTLNAW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Donor MHC A3, A28, B53, B57; A31, B7, B57
Assay type Chromium-release assay
Keywords TCR usage, genital and mucosal immunity
References Musey *et al.* 2003

- CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCR? VDJ region sequencing revealed cases of expansion of the same clone in different compartments.
- CD8+ T cell clones directed at this epitope were derived from blood and semen of one male subject, and blood and cervix of one female subject.
- From the male patient, six clones that recognized this epitope had three different patterns of TCR? usage: 2 from the blood and 1 from the semen used Vβ6S2DJ2S2; 1 from the blood and 1 from the semen used Vβ6S2DJ1.1; and 1 from the semen used Vβ7S1DJ2.3.
- From the female patient, five clones that recognized this epitope had different TCR? usage. Blood derived clones were B?6S7DJ2.7, B?6.4DJ2.3, and B?6S3DJ2.1. Cervix derived clones were B?6S3DJ1.4 and B?6S5DJ2.5.

HXB2 Location p24 (15–23)
Author Location Gag (147–155)
Epitope ISPRTLNAW
Epitope name ISW9
Subtype B, C
Immunogen HIV-1 infection
Species (MHC) human (B57)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords epitope processing, escape
References Draenert *et al.* 2004b

- The A146P mutation flanking the ISW9 epitope (Pisprtlnaw) is positively selected in HLA-B57+ persons and it prevents trimming of the optimal epitope by the endoplasmic reticulum aminopeptidase I. The A146P processing escape mutation does not influence replicative capacity of the virus in vitro and is accumulated over time in the human population.

HXB2 Location p24 (15–23)
Author Location p24 (15–23)
Epitope ISPRTLNAW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 3/7 patients recognized this epitope.

HXB2 Location p24 (15–23)
Author Location (147–155 B consensus)
Epitope ISPRTLNAW
Epitope name IW9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords characterizing CD8+ T cell responses
References Allen *et al.* 2004

- This study characterizes an escape mutation in a C-terminal flanking residue of the HLA-A3 gag p17 KK9 epitope that inhibits processing, and is embedded in the overlapping HLA-A3 RK9 epitope.
- The immune response was tracked in subject AC-38. The acute immunodominant response was to the B57 TW10 epitope; this response declined following viral escape (tsNlqeqigw) by day 64. The p17 KK9 and RK9 became immunodominant, but then declined as the escape mutation arose. IW9 is one of three other strong responses and that persisted, along with one sub-dominant response.

HXB2 Location p24 (15–23)
Author Location p24
Epitope ISPRTLNAW
Epitope name ISW9
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords review, epitope processing, escape
References Goulder & Watkins 2004

- This paper is a review of the role of CTL in HIV infection, and it uses the ISW9 epitope as an example of an epitope that escapes due to a mutation before the N-terminal end of the epitope. The insertion of a proline prevents the aminopeptidase ERAAP from cleaving the glutamine from the precursor, qPisrptlnaw, preventing processing of ISRPTLNAW.

HXB2 Location p24 (15–23)
Author Location p24 (147–155 IIIB)
Epitope ISPRTLNAW
Immunogen HIV-1 infection
Species (MHC) human (B57, B*5801)
Keywords rate of progression
References Goulder *et al.* 1996b

- Five slow progressors made a response to this epitope, and in two it was the dominant response.
- Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations.

HXB2 Location p24 (15–23)

Author Location p24 (subtype A)
Epitope LSPRTLNAW
Subtype A
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B57, B58)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location p24 (15–23)
Author Location p24 (147–155)
Epitope LSPRTLNAW
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B57, B58)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- Variants (L/I)SPRTLNAW are specific for the A/B clades.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B57/B58 women, 4/6 HEPS and 14/17 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in 2 of the 4/6 HEPS cases and in 7 of the 14/17 responsive HIV-1 infected women.

HXB2 Location p24 (16–24)
Author Location p24
Epitope SPRTLNAWV
Immunogen HIV-1 infection
Species (MHC) chimpanzee
References Santra *et al.* 1999

- 3/4 animals displayed HIV-1 Gag-specific CTL activity.
- Effector cells from two chimpanzees were able to recognize epitopes also recognized by human HIV-1 Gag-specific CTL (SPRTLNAWV, HLA-B7, and DLNTMLNTV, HLA-B14)
- No chimpanzee CTL were detected to the following human HIV-1 specific Gag epitopes, although they were embedded within 20mer peptides that contained a reactive epitope: ISPRTLNAW, HLA-B57; KRWIILGLNK, HLA-B27; and DRFYKTLRA, HLA-B14.

HXB2 Location p24 (16–24)
Author Location p24 (148–156)
Epitope SPRTLNAWV
Immunogen
Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0702 epitope.
- Optimal peptide mapped by titration.

HXB2 Location p24 (16–24)
Author Location p24 (148–156)
Epitope SPRTLNAWV
Immunogen
Species (MHC) human (B7)
References Brander & Walker 1997

- Optimal peptide mapped by titration, pers. comm. from D. Lewinsohn to C. Brander and B. Walker.

HXB2 Location p24 (16–24)
Author Location p24 (148–156)
Epitope SPRTLNAWV
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Brodie *et al.* 2000

- Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL.
- Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication.
- The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism.
- This study provides a methodology for tracking and studying antigen specific CTL *in vivo*.

HXB2 Location p24 (16–24)
Author Location p24 (148–156)
Epitope SPRTLNAWV
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B7)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.

- Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGVIRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.

HXB2 Location p24 (16–24)
Author Location p24 (16–24)
Epitope SPRTLNAWV
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP).
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location p24 (16–24)
Author Location
Epitope SPRTLNAWV
Epitope name Gag-SW9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B07, 1/9 (11%) recognized this epitope.
- Among HIV+ individuals who carried HLA B81, 1/6 (17%) recognized this epitope.

HXB2 Location p24 (16–24)
Author Location p24 (16–24)
Epitope SPRTLNAWV
Epitope name B7-SV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 1/11 HLA-B7 positive individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.

HXB2 Location p24 (16–24)
Author Location p24 (16–24)
Epitope SPRTLNAWV
Epitope name B7-SV9 Gag
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response, but in this case the epitope did not vary.

HXB2 Location p24 (16–24)
Author Location p24 (148–156)
Epitope SPRTLNAWV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- None of seven patients responded to this peptide with GzB producing cells or IFN-gamma producing cells.
- The authors describe the epitope as SPRTLNNQWV – the double N's may be a typo or an unusual form of the epitope; it is atypical and may be why there was no response.

HXB2 Location p24 (16–24)
Author Location p24 (16–24)
Epitope SPRTLNAWV
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay

Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 7 patients recognized this epitope.

HXB2 Location p24 (16–24)
Author Location p24 (subtype B)
Epitope SPRTLNAWV
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B7, B*8101)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location p24 (16–24)
Author Location Gag (subtype B)
Epitope SPRTLNAWV
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B7, B*8101)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among A, B, and D clade viruses.

HXB2 Location p24 (18–26)
Author Location Gag (150–)
Epitope RTLNAWVKV
Epitope name Gag150
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was an intermediate A2 binder, and induced CTL responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.

HXB2 Location p24 (19–27)
Author Location p24 (151–159)
Epitope TLNAWVKVV
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords HAART, ART, immunodominance
References Huang *et al.* 2000

- The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed.
- Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT.
- In 3/3 HLA-A*02, -B*27 subjects the immunodominant epitope was against HLA B*27 Gag p24 epitope KRWIILGL, not A2 Gag epitopes.

HXB2 Location p24 (19–27)
Author Location p24 (151–159)
Epitope TLNAWVKVV
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords HAART, ART
References Rinaldo *et al.* 2000

- Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that can persist after therapy and long periods of virus being below the level of detection.

HXB2 Location p24 (19–27)
Author Location p24 (151–159)
Epitope TLNAWVKVV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Parker *et al.* 1992; Parker *et al.* 1994

- Study of sequence motifs preferred for peptide binding to class I HLA-A2.

HXB2 Location p24 (19–27)
Author Location p24 (19–27)
Epitope TLNAWVKVV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (19–27)
Author Location p24 (150–159)
Epitope TLNAWVKVI
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A2)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- Variants TLNAWVKV(I/V) are A/B clade specific.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location p24 (19–27)
Author Location p24 (A02, A30, B4402, B15)
Epitope TLNAWVKVV
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords HIV exposed persistently seronegative (HEPS), characterizing CD8+ T cell responses
References Missale *et al.* 2004

- HIV-specific T-cell response was tested in HIV-uninfected patients exposed to blood from a patient with highly replicating HIV; these same patients were nosocomially infected with HBV. HIV-specific T-cell responses were directed to structural and non-structural HIV proteins in two patients suggesting that the virus replicated in these patients sufficiently to prime a cell-mediated immune response that protected these individuals from HIV infection.
- This patient responded to 4/8 HIV epitopes tested in an IFNgamma EliSpot assay or tetramer assay. Responses were detected to this peptide 8 and 28 weeks after exposure with EliSpot, but not by tetramer binding.

HXB2 Location p24 (19–27)
Author Location p24 (subtype B)
Epitope TLNAWVKVV
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2, A*0202)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among A, B and D clade viruses.

HXB2 Location p24 (21–30)
Author Location Gag (153–162 WEAU)
Epitope NAWVKIEEK
Epitope name Gag NK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- There was a weak response to this epitope during acute and early infection, and the epitope sequence did not vary during the first year of the infection.

HXB2 Location p24 (21–40)
Author Location p24 (153–172 SF2)
Epitope NAWVKVVEEKAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A2, -B21.

HXB2 Location p24 (21–40)
Author Location p24 (153–172 SF2)
Epitope NAWVKVVEEKAFSPEVIPMF
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* CD4BS, Gag, gp120, V3
Species (MHC) macaque
References Wagner *et al.* 1998b

- A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock Wagner *et al.* [1998b]
- CTL specific for this epitope could be found both before and after SHIV challenge.

HXB2 Location p24 (21–40)
Author Location Gag (153–172)
Epitope NAWVKVVEEKAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Brodie *et al.* 1999

- The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptively transferring them.
- The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects.

HXB2 Location p24 (21–40)
Author Location p24 (153–172)
Epitope NAWVKVVEEKAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Brodie *et al.* 2000

- Study tracks and quantifies *in vivo* migration of neo-marked CD8+ HIV-specific CTL.
- Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication.
- The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1? and MIP-1?, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism.
- This study provides a methodology for tracking and studying antigen specific CTL *in vivo*.

HXB2 Location p24 (21–42)
Author Location p24 (153–174 BH10)
Epitope NAWVKVVEEKAFSPEVIPMFSA
Immunogen HIV-1 infection
Species (MHC) human (Bw57)
References Johnson *et al.* 1991

- Gag CTL response studied in three individuals.

HXB2 Location p24 (24–32)
Author Location (C consensus)
Epitope VKVIEEKAF
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (28–36)
Author Location p24
Epitope EEKAFSPEV
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (B*4415)
Keywords HIV exposed persistently seronegative (HEPS)
References Bird *et al.* 2002

- 5/233, (4 HIV-1 positive, 1 HEPS) (2.1%) Kenyan female sex workers carried the novel HLA allele B*4415.
- Residues forming the B pocket of HLA B*4415 were identical to HLA B*4001, B*4402 and B*4403. These alleles preferred E, an acidic residue, at the P2 position.
- The amino acid residues forming the F pocket of allele B*4415 were not correlated with other known HLA molecules, but analogy suggests a binding preference for small, neutral amino acids.
- Based on the binding motif x[DE]xxxxxx[VILA], 19 potential B*4415 epitopes were identified, and 1/19 was reactive in an Elispot, EEKAFSPEV.

HXB2 Location p24 (28–36)
Author Location p24 (28–36)
Epitope EEKAFSPEV
Immunogen
Species (MHC) human (B*4415)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p24 (28–36)
Author Location (C consensus)
Epitope EEKAFSPEV
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*4501)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (28–47)
Author Location p24 (160–179)
Epitope EEKAFSPEVIPMFSALSEGA
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Musey *et al.* 1997
- Cervical and peripheral blood derived CTL clones from an HIV-infected woman recognized this epitope.

HXB2 Location p24 (29–48)
Author Location Gag (161–180 C consensus)
Epitope EKAFSPEVPMFTALSEGAT
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002
- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location p24 (30–37)
Author Location p24 (162–170 LAI)
Epitope KAFSPEVI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5703)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*5703 epitope.

HXB2 Location p24 (30–37)
Author Location p24 (30–37)
Epitope KAFSPEVI
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Goulder *et al.* 2000c
- Two strong clonal CTL responses were generated in donor 026-BMC (HLA A3/-, B42/B57, Cw7/17) against different optimal versions of this epitope, one 8 amino acids long, one 11.
- Improved stabilization of the B57-peptide complex was demonstrated by the 11 mer which fits the B57 binding motif, relative to the 8 mer, which does not.
- B57 tolerates marked difference in optimal peptide length – and B57 is associated with non-progressive infection.

HXB2 Location p24 (30–37)
Author Location
Epitope KAFSPEVI
Epitope name Gag-KI8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Sabbaj *et al.* 2002b
- Among HIV+ individuals tested who carried HLA B57, 0/5 (0%) recognized this epitope.

HXB2 Location p24 (30–40)
Author Location p24
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c
- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized by 1/22 HEPS sex worker controls, ML1250.

HXB2 Location p24 (30–40)
Author Location p24
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B*57)
Keywords HAART, ART
References Spiegel *et al.* 1999
- Study examines the effect of highly active antiretroviral therapy (HAART) on HIV-1 plasma viral load, CTLp and CTLe frequencies in 8 infected children.
- CTLp (precursors) were measured by stimulating in culture and assaying using 51Cr release, against vaccina expressed IIIB Env, Gag, Pol, Nef, and CTLe were measured by ELISPOT.
- CTL against B*57-KAFSPEVIPMF was a de novo response observed in one of the children when viral load increased as a result of stopping therapy.
- HIV-1 specific CTL responses initially increased in children with complete viral suppression, but then decreased, suggesting viral replication is needed to maintain CTL responses.

HXB2 Location p24 (30–40)
Author Location p24 (162–172 LAI)
Epitope KAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords rate of progression

References Goulder *et al.* 1996b

- This peptide was recognized by CTL from five slow progressors.
- Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations.
- This epitope is highly conserved.

HXB2 Location p24 (30–40)
Author Location p24 (162–172 LAI)
Epitope KAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5701 epitope.

HXB2 Location p24 (30–40)
Author Location
Epitope KAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords rate of progression, immunodominance
References Migueles & Connors 2001

- HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.
- Attempts to make all for HLA B*5701-epitope tetramers were made, but only the HLA B*5701-KAFSPEVIPMF tetramer folded properly. The percentage of CD8+ T cells staining with this HLA B*57 gag tetramer and the fraction of CD69+IFN-+ cells responding to autologous B cells pulsed with KAFSPEVIPMF was highly correlated ($r = 0.84$; $P = 0.005$). The percent of CD8+ T cells that stain with the A*2 gag SLYNTVATL tetramer was low (0-0.31%) in a A2+ B57+ LTNP, emphasizing the focus of the immune response on the B*5701 epitopes.

HXB2 Location p24 (30–40)
Author Location
Epitope KAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords rate of progression, immunodominance
References Migueles & Connors 2001

- CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.
- CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia.
- The HLA-A*0201 SLYNTVATL epitope response was not as strong in individuals that carried both A2 and B57.

HXB2 Location p24 (30–40)
Author Location Gag (162–172)
Epitope KAFSPEVIPMF
Epitope name KAF11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Assay type Intracellular cytokine staining, Flow cytometric CTL assay
Keywords rate of progression, escape
References Migueles *et al.* 2003

- cDNA Gag sequences from a set of 17 HLA-B*5701+ progressors and 10 LTNPs were obtained, and the variation in four p24 B*5701 epitopes examined. Sequence variants were more common ($p < 0.01$) in the epitopes in the progressors (median 3, range 1-7) than LTNPs (median 2, range 0-4).
- In general, use of the autologous protein in a target cell did not diminish the overall CD8+ T-cell responses.
- This epitope tends to be quantitatively immunodominant in B57+ people, including in some of the individuals in this study. It was extremely well conserved in the sequences obtained here, despite strong immune pressure, suggesting fitness constraints.

HXB2 Location p24 (30–40)
Author Location p24 (30–40)
Epitope KAFSPEVIPMF
Epitope name KAFS
Subtype A, B
Immunogen HIV-1 infection
Species (MHC) human (B*5701, B*5703)
Keywords inter-clade comparisons, rate of progression
References Gillespie *et al.* 2002

- CTL responses of eight HIV+ slow progressors from Nairobi Kenya or Oxford, UK who were B*5701 or B*5703 were studied, as B*57 is associated with slow progression.
- This epitope is located between the structurally conserved alpha-helix 1 and alpha-helix 2 (H1-H2) region of the p24 capsid protein, and tends to elicit strong reactions in B*57 individuals.
- Broad heterogeneous cross-clade reactivity to 6 clade variants of the KAFS peptide sequence were observed in one B*5701 and 5 B*5703 HLA-restricted patients, measured by IFNγ production Elispot assays as well as tetramer binding. The clade variants were: KAFSPEVIPMF (clades A and B), kGfNpevipmf (clades A/AC); kaLspevipmf (clade A); kafspevipVf (clade A); kafNpeIipmf (group O); kafspeIipmf (A/C); kafsQevipmf (A/C); and kaLspevipmf KNFSPEVIPMF A/G). Not all variants were well recognized in all patients, for example kafsQevipmf was not able to induce IFN gamma production in 3/6 tested, and had a diminished capacity to sensitize target cells for lysis.

HXB2 Location p24 (30–40)
Author Location p24 (162–172 LAI)
Epitope KAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5703)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5703 epitope.

HXB2 Location p24 (30–40)
Author Location
Epitope KAFSPEVIPMF
Epitope name Gag-KF11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5703)
Donor MHC A*3402 A*7401 B*0801 B*5703 Cw*0302 Cw*0701
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subject 00RCH59 was African American, on HAART, viral load 170, CD4 count 477.
- Among HIV+ individuals who carried HLA-B57, 6/6 (100%) recognized this epitope.

HXB2 Location p24 (30–40)
Author Location p24 (30–40)
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Goulder *et al.* 2000c

- Two strong clonal CTL responses were generated in donor 026-BMC (HLA A3/-, B42/B57, Cw7/17) against different optimal versions of this epitope, one 8 amino acids long, one 11.
- Improved stabilization of the B57-peptide complex was demonstrated by the 11mer which fits the B57 binding motif, relative to the 8 mer, which does not.
- B57 tolerates marked difference in optimal peptide length – and B57 is associated with non-progressive infection.

HXB2 Location p24 (30–40)
Author Location p24 (162–172)
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others.

HXB2 Location p24 (30–40)
Author Location p24 (SF2)
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope is not among the most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p24 (30–40)
Author Location Gag (SF2)
Epitope KAFSPEVIPMF
Epitope name KF11
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Goulder *et al.* 2001a

- Three CTL responses in patient PI004, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.

HXB2 Location p24 (30–40)
Author Location p24 (162–172)
Epitope KAFSPEVIPMF
Epitope name KAF
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- None of the 8 study subjects recognized this epitope but none were HLA B57+.

HXB2 Location p24 (30–40)
Author Location p24
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Kostense *et al.* 2001

- HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load.
- Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional.
- In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival.

HXB2 Location p24 (30–40)
Author Location p24 (162–172 SF2)
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 2/2 group 3.

HXB2 Location p24 (30–40)
Author Location p24 (163–174)
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Appay *et al.* 2000

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α.

HXB2 Location p24 (30–40)
Author Location
Epitope KAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B57, 1/5 (20%) recognized this epitope.

HXB2 Location p24 (30–40)
Author Location p24
Epitope KAFSPEVIPMF
Epitope name KAF
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFN? Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location p24 (30–40)
Author Location p24 (30–40)
Epitope KAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
Donor MHC A*0201, A3, B44, B57, Cw5, Cw6
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- Alleles A3, B35, B57, and B62 were more frequently recognized than alleles A1, A2, A30, and A44 e.g., during primary infection. 2/10 patients, 1372 and 1397, recognized A2-restricted epitopes. The common A2-restricted epitopes Gag SL9 and Pol IV9 were not recognized in peptide tetramer-binding assays.

HXB2 Location p24 (30–40)
Author Location p24
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
Assay type Intracellular cytokine staining
Keywords immunodominance, genital and mucosal immunity
References Kaul *et al.* 2003

- Predefined immunodominant peptide responses were used to compare CD8+ T-cell responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T-cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher.
- The immunodominant response was to this epitope in the PBMC of 10/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).

HXB2 Location p24 (30–40)
Author Location p24 (163–174)
Epitope KAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
Donor MHC A0201, A3, B57, C06, C07 and A01, A0201, B08, B57, C6, C7
Country United States.
Assay type cytokine production, Tetramer binding, Intracellular cytokine staining, Degranulation, CD107a and b cell surface mobilization
Keywords TCR usage
References Betts *et al.* 2004

- Both cytokine production and degranulation in HIV-1 specific and CMV specific CD8+ T -cells occurs at high peptide concentrations together with TCR downregulation. Only degranulation is observed at lower peptide concentrations with no observed TCR downregulation. Thus the nature of CTL response depends not on the specific T cell clonotype or antigen, but on the concentration of Ag presented on APCs.

HXB2 Location p24 (30–40)
Author Location p24
Epitope KAFSPEVIPMF
Epitope name TW10
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B57)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords epitope processing, escape
References Draenert *et al.* 2004b

- This study characterizes the N-terminal flanking position of the epitope ISPRTLNAW, and mutations in this position are thought to impact processing. The B57 epitope KAFSPEVIPMF was used as a positive control in this study.

HXB2 Location p24 (30–40)
Author Location Gag (155–172 B con)
Epitope KAFSPEVIPMF
Epitope name KF11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords variant cross-recognition or cross-neutralization
References Draenert *et al.* 2004c

- CD8+ T-cell responses that persisted in individuals with advanced disease were studied; most of the optimal epitopes defined were recognized with intermediate to high avidity. On average 13 (range, 2-39) epitopic regions were targeted in an average of 6 proteins (range, 1-8). HAART resulted in decrease in antigen and reduction in gamma IFN EliSpot responses, suggesting active responses to autologous virus. Limited or no mutations within most viral epitopes suggest that persistent CTL through late disease do not exert strong immune selection pressure, yet the Elispot assays show robust responses, suggesting to the authors that gamma IFN based screening methods may not reveal functional CD8+ T-cell impairment in patients with AIDS.
- Two subjects recognized this epitope, one with high functional avidity, one with intermediate. Autologous sequence revelaed no substitutions in this epitope compared to the B consensus.

HXB2 Location p24 (30–40)
Author Location Gag
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- 1/2 HLA B57+ infection-resistant men, compared to 0/1 preseroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location p24 (30–40)
Author Location p24 (30–40)
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI)
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 7/7 patients recognized this epitope.

HXB2 Location p24 (30–40)
Author Location (162–172 B consensus)

Epitope KAFSPEVIPMF
Epitope name KF11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords immunodominance, characterizing CD8+ T cell responses
References Allen *et al.* 2004

- This study characterizes an escape mutation in a C-terminal flanking residue of the HLA-A3 gag p17 KK9 epitope that inhibits processing, and is embedded in the overlapping HLA-A3 RK9 epitope.
- The immune response was tracked in subject AC-38. The acute immunodominant response was to the B57 TW10 epitope; this response declined following viral escape (tsNlqeqigw) by day 64. The p17 KK9 and RK9 became immunodominant, but then declined as the escape mutation arose. FK11 is one of three other strong responses and that persisted, along with one sub-dominant response.

HXB2 Location p24 (30–40)
Author Location (C consensus)
Epitope KAFSPEVIPMF
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (30–40)
Author Location p24
Epitope KAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country United Kingdom.
Assay type Tetramer binding, T-cell Elispot, Intracellular cytokine staining
Keywords rate of progression, acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Papagno *et al.* 2004

- Acute HIV-1 infection induces massive activation of HIV-specific and non-HIV-specific CD8+ T-cells resulting in differentiation of these cells. High differentiation of CD8+ T-cells is correlated with disease progression. Differentiation is a natural process but it can be driven by elevated immune activation, such as in HIV infection.

HXB2 Location p24 (30–40)
Author Location p24 (153–164)
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B57, B58)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B57/B58 women, 4/6 HEPS and 12/17 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in 2 of the 4/6 HEPS cases and in 7 of the 12/17 HIV-1 infected women.

HXB2 Location p24 (30–40)
Author Location p24 (30–40)
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57, B58)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002

- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.
- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location p24 (30–40)
Author Location p24 (30–40)
Epitope KAFSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B58)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (31–44)
Author Location p24 (31–44 HXB2)
Epitope AFSPEVIPMFSALS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided, it appears to be HXB2.
- Responses to this peptide were detected in 22% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (31–50)
Author Location p24 (163–182)
Epitope AFSPEVIPMFSALSEGATPQ
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location p24 (31–50)
Author Location p24 (163–182 SF2)
Epitope AFSPEVIPMFSALSEGATPQ
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A2, B21.

HXB2 Location p24 (31–50)
Author Location p24 (163–182 SF2)
Epitope AFSPEVIPMFSALSEGATPQ
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location p24 (31–50)
Author Location p24 (SF2)
Epitope AFSPEVIPMFSALSEGATPQ
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.
- The response to the peptide was CD4 dependent, but the HLA presenting molecule and optimal epitope were not determined.

HXB2 Location p24 (32–40)
Author Location Gag (164–172)
Epitope FSPEVIPMF
Immunogen HIV-1 infection
Species (MHC) human (B57)
Donor MHC A3, A28, B53, B57
Assay type Chromium-release assay
Keywords TCR usage, genital and mucosal immunity
References Musey *et al.* 2003

- CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCR? VDJ region sequencing revealed cases of expansion of the same clone in different compartments.
- CD8+ T cell clones directed at this epitope were derived from blood and semen.
- The TCR? VDJ rearrangement of a CTL clone from the blood was Vβ21S3DJ1.2, and a clone from the semen used Vβ7S1DJ2.3.

HXB2 Location p24 (35–43)
Author Location p24 (167–175 LAI)
Epitope EVIPMFSAL
Subtype B
Immunogen
Species (MHC) human (A*2601)
Keywords inter-clade comparisons
References Goulder *et al.* 1996a

- Identified as optimal epitope within Gag sequence AFSPEVIPMFSALSEGATPQ.
- Relatively conserved epitope within B clade and in other clades.
- Suspected binding motif for HLA-A26 includes T or V anchor at position 2, negative charge at position 1.
- C. Brander notes that this is an A*2601 epitope in the 1999 database.

HXB2 Location p24 (35–43)
Author Location p24 (167–175 LAI)

Epitope EVIPMFSAL
Subtype B
Immunogen
Species (MHC) human (A*2601)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes that this is an A*2601.

HXB2 Location p24 (35–43)
Author Location p24 (167–175)
Epitope EVIPMFSAL
Immunogen HIV-1 infection
Species (MHC) human (A26)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope.

HXB2 Location p24 (35–43)
Author Location Gag
Epitope EVIPMFSAL
Epitope name EL9
Immunogen HIV-1 infection
Species (MHC) human (A26)
Donor MHC A26, B27
Assay type CD8 T-cell Elispot - IFNγ
Keywords responses in children, rate of progression, immunodominance, escape
References Feeney *et al.* 2004

- Viral load in a perinatally infected child remained low until emergence of an escape variant (kTwiilglnk) in the immunodominant CTL epitope KRWIILGLNK when the child was 7.4 years old. The emergence of this escape mutation was followed by an increase in viremia and an increase in the number of targeted CTL epitopes, measured again when the child was 9.2 years old. The EL9 response was not observed until after the escape mutation occurred in the immunodominant epitope, and was detected in the 9.2 year sample for the first time.

HXB2 Location p24 (35–49)
Author Location p24 (35–48 HXB2)
Epitope EVIPMFSALSEGATP
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (36–43)
Author Location p24 (168–175 LAI)
Epitope VIPMFSAL
Subtype B
Immunogen
Species (MHC) human (Cw*0102 (Cw1))
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a C*0102(Cw1) epitope.

HXB2 Location p24 (36–43)
Author Location p24 (168–175 LAI)
Epitope VIPMFSAL
Subtype B
Immunogen
Species (MHC) human (Cw*0102, Cw1)
References Goulder *et al.* 1997b

HXB2 Location p24 (36–43)
Author Location p24 (168–175)
Epitope VIPMFSAL
Immunogen HIV-1 infection
Species (MHC) human (Cw1, Cw2)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope.

HXB2 Location p24 (37–52)
Author Location Gag (169–184 LAI)
Epitope IPMFSALSEGATPQDL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B12)
References Buseyne *et al.* 1993a

- Vertical transmission of HIV ranges from 13% to 39%
- Primary assays showed that cytotoxic activity against at least one HIV protein was detected in 70% of infected children.

- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM17 (CDC P2A+C+D2) had a CTL response to two epitopes in Gag.

HXB2 Location p24 (37–52)
Author Location p24 (169–184 LAI)
Epitope IPMFSALSEGATPQDL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B12(44))
References Buseyne *et al.* 1993b

- Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.

HXB2 Location p24 (37–52)
Author Location p24 (37–52)
Epitope IPMFSALSEGATPDQL
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (39–58)
Author Location Gag (171–190)
Epitope MFTALSEGTPQDLNTMLNT
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location p24 (41–60)
Author Location p24 (173–192 SF2)
Epitope SALSEGATPQDLNTMLNTVG
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- Three of these 12 had CTL response to this peptide.
- The responding subjects were HLA-A3, A32, B7, B14; and HLA-A2, A3, B14, B44.

HXB2 Location p24 (41–60)
Author Location p24 (173–192 SF2)
Epitope SALSEGATPQDLNTMLNTVG
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location p24 (41–60)
Author Location p24 (SF2)
Epitope SALSEGATPQDLNTMLNTVG
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.
- The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.

HXB2 Location p24 (41–60)
Author Location p24 (179–188 subtype A)
Epitope SALSEGATPQDLNMMLNIVG
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (B*8101)
Keywords inter-clade comparisons
References Dorrell *et al.* 1999

- CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa.
- This CTL epitope is presented by B*8101 in one of the patients with an A subtype infection – B*8101 is a newly discovered HLA allele found in Africans, and the epitope has yet to be mapped precisely.
- This epitope is distinct in subtype A relative to subtypes B, C, and D which share the dominant sequence: SALSEGATPQDL-NTMLNTVG.

HXB2 Location p24 (41–62)
Author Location p24 (173–194 BH10)
Epitope SALSEGATPQDLNTMLNTVGGH
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Johnson *et al.* 1991

- Gag CTL response studied in three individuals.

HXB2 Location p24 (43–52)
Author Location Gag (175–184 WEAU)
Epitope LSEGATPQDL
Epitope name Gag LL10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4403)
Donor MHC A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- There was a weak response to this epitope during acute and early infection, and the epitope sequence did not vary during the first year of the infection.

HXB2 Location p24 (43–52)
Author Location p24 (subtype A)
Epitope LSEGATPQDL
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (B42, B44)
Keywords inter-clade comparisons
References Cao *et al.* 2000

- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D.
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.
- This optimal epitope sequence, recognized by CTL derived from a Ugandan with an A subtype infection (patient SP 511), is cross-reactive with subtypes A, B and D peptides.

HXB2 Location p24 (44–52)
Author Location p24 (176–184)
Epitope SEGATPQDL
Immunogen
Species (MHC) human (B*4001)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4001, B60 epitope.

HXB2 Location p24 (44–52)
Author Location p24
Epitope SEGATPQDL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (B60)
Donor MHC A2, A24, B38, B60, Cw2, Cw12
Assay type CD8 T-cell Elispot - IFNγ
Keywords HAART, ART, supervised treatment interruptions (STI), acute infection, early treatment
References Montefiori *et al.* 2003

- HIV-1 + patient AC10 underwent early HAART treatment, which was discontinued 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.

HXB2 Location p24 (44–52)
Author Location p24 (44–52 NL43)
Epitope SEGATPQDL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B60)
Assay type Chromium-release assay, CTL suppression of replication
Keywords escape
References Yang *et al.* 2003a

- Virus was cultured in the presence of CTL lines specific for 5 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, SEGATPQDL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts.
- One CTL clone, 161Jx12, recognized this epitope, and apparently no resistance mutations were selected by this clone, although the data was not shown in the paper.

HXB2 Location p24 (44–52)
Author Location p24 (176–184)
Epitope SEGATPQDL
Epitope name Gag/p24-SL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B60)
Assay type Chromium-release assay
Keywords binding affinity, TCR usage, characterizing CD8+ T cell responses
References Yang *et al.* 2003b

- Killing efficiency of CTLs and their ability to suppress viral replication is shown to depend more on epitope specificity than to antigenic avidity. Different clones recognizing the same epitope had similar killing efficiency despite their variation in avidity. Nef specific CTL clones tended to be most inhibitory, followed by Gag, then by RT specific clones, regardless of avidity.
- 1/14 CTL T-cell clones tested were specific for Gag/p24-SL9. Under conditions of excess peptide (100ug/ml), there was no difference in their lytic potential; all possessed similar effector capacity. Avidity was measured as the sensitizing dose of peptide required for 50% of maximal killing (SD50), which varied

from 20 pg/ml to 100 ng/ml, over four orders of magnitude for all 14 epitopes. The SD50 value for Gag/p24-SL9 was 30 pg/ml, it was among the peptides with the highest avidity.

HXB2 Location p24 (44–52)
Author Location p24 (HXB2)
Epitope SEGATPQDL
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (B60)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords epitope processing, vaccine antigen design, characterizing CD8+ T cell responses
References SenGupta *et al.* 2004

- Multiple HLA calss I-restricted and class II-restricted T-cell epitopes were shown to be processed and presented from an exogenously added HIV-1 gag-p24 peptide complexed to a heat shock protein. T-cell recognition of the complex was shown to be inhibited by brefeldin A indicating an endoplasmic reticulum-dependent pathway.

HXB2 Location p24 (44–52)
Author Location p24 (SF2)
Epitope SEGATPQDL
Immunogen HIV-1 infection
Species (MHC) human (B60, B*4001)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes.
- B60 is present in 10-20% of the Caucasoid and very common in Asian populations.

HXB2 Location p24 (44–52)
Author Location p24 (44–52)
Epitope SEGATPQDL
Immunogen HIV-1 infection
Species (MHC) human (B60, B61)
Keywords immunodominance
References Day *et al.* 2001

- No immunodominant responses were detected to five B61-restricted epitopes tested.
- All five B60-restricted epitopes were reactive in another subject, the strongest CTL response directed against the B60-epitope p24 SEGATPQDL, and the B60-restricted responses together contributed over one-third of the total CTL response.

HXB2 Location p24 (46–59)
Author Location p24 (SF2)
Epitope GATPQDLNTMLNTV
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ African American living in Boston with HLA A*3002/68 B14/*5802 Cw6/8 – this epitope fell within the most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects from South Africa.

HXB2 Location p24 (47–55)
Author Location p24 (47–55)
Epitope ATPQDLNTM
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (47–56)
Author Location p24 (subtype A)
Epitope ATPQDLNMML
Subtype A
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B53)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T-cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T-cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T-cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location p24 (47–58)
Author Location p24 (181–192)
Epitope CTPYDINQMLNC
Immunogen HIV-2 infection
Species (MHC) human (B58)
References Bertoletti 1998

- HIV-2 epitope defined from an infection in Gambia, Bertoletti, pers. comm.

HXB2 Location p24 (48–55)
Author Location p24 (48–55)
Epitope TPQDLNTM
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 7 patients recognized this epitope.

HXB2 Location p24 (48–56)
Author Location Gag
Epitope TPQDLNTML
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement, epitope processing, characterizing CD8+ T cell responses
References Beattie *et al.* 2004

- This study compared CD8+ T-cell EliSpot reponses to 58 Gag peptides that were optimal epitopes, with responses to overlapping 15 mers that spanned Gag. When screening for HIV-1-specific CD8+ T-cell responses from 49 HIV+ people, overlapping 15-mer peptide pools revealed several novel responses that would have been missed using predefined CD8 epitopes. However, the 15-mer pools often missed low-level responses to predefined epitopes, especially when the epitope was located centrally in the 15-mer peptide, and the overall level of response to the 15 mers was generally lower(mean 1.4 five fold dilutions lower, range 0-3).
- The response to TPQDLNTML was used as an example of a titration curve. When comparing the peptide TPQDLNTML to the 15 mer EGATPQDLNTMLNTV, the 15 mer had a diminished response to the same amount of peptide.

HXB2 Location p24 (48–56)
Author Location Gag (96ZM651.8)
Epitope TPQDLNTML
Epitope name G180-TL9
Immunogen
Species (MHC) human (A*4201, B*8101)
Keywords inter-clade comparisons, immunodominance
References Novitsky *et al.* 2001

- This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort.
- 19/46 (41.3%) had CTL responses to one or more peptides within the first immunodominant region of Gag (peptides TLNAWVKVIEEKAFSPEVIP, EKAFSPEVIPMFTALSEGAT, and MFTALSEGATPQDLNTMLNT), with magnitudes of response with ELISPOT results median and range 495 (103 to 1,447) SFC/10^6 PBMC
- 7/11 HLA-A*4201+ subjects (64%) responded to peptide MFTALSEGATPQDLNTMLNT.
- TPQDLNTML is a A*4201 epitope within TLNAWVKVIEEKAFSPEVIP.

HXB2 Location p24 (48–56)
Author Location p24 (180–188 IIIB)
Epitope TPQDLNTML
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0702 epitope.

HXB2 Location p24 (48–56)
Author Location p24 (179–187 LAI)
Epitope TPQDLNTML
Subtype B
Immunogen
Species (MHC) human (B*4201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4201 epitope.

HXB2 Location p24 (48–56)
Author Location p24
Epitope TPQDLNTML
Epitope name TL-9
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*4201, B*8101)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, epitope processing, immunodominance, cross-presentation by different HLA
References Masemola *et al.* 2004b

- Highly targeted regions in Gag for CD8+ T-cells were defined for individuals with C clade infections in South Africa. Nine specific epitopes within the most reactive regions were characterized. Some epitopes were shown to be promiscuous, presented by multiple class I restricting alleles.
- TPQDLNTML was presented by B*4201 and B*8101. B*44 is more common among Caucasians than Zulus (allele frequency 0.149 versus 0.107), while A*29 is more common in Zulus (0.045 versus 0.125). This epitope had previously identified in B clade infections.

HXB2 Location p24 (48–56)
Author Location Gag (173–181 HIV-2)
Epitope TPYDINQML
Immunogen HIV-2 infection
Species (MHC) human (B*5301)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5301 epitope.

HXB2 Location p24 (48–56)
Author Location p24 (180–188 LAI)
Epitope TPQDLNTML
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*8101)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*8101 epitope.

HXB2 Location p24 (48–56)
Author Location
Epitope TPQDLNTML
Epitope name Gag-TL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*8101, B*5301, B7)
Donor MHC A*3402 A*7401 B*5301 B*8101 Cw*0401 Cw*0802
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subjects 00RCH86 and 03RCH59 both recognized this epitope, both restricted by HLA B*8101.
- Subject 00RCH86 was African American, not on HAART, viral load 51000, CD4 count 520.
- Subject 03RCH59 was African American, male, on HAART, viral load 22000, CD4 count 769.
- Among HIV+ individuals who carried HLA B07, 2/9 (22%) recognized this epitope.
- Among HIV+ individuals who carried HLA B*5301, 3/15 (20%) recognized this epitope.
- Among HIV+ individuals who carried HLA B81, 4/6 (67%) recognized this epitope.

HXB2 Location p24 (48–56)
Author Location (C consensus)
Epitope TPQDLNTML
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B39, B*4201, B*8101, Cw*0802)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (48–56)
Author Location p24 (C consensus)
Epitope TPQDLNTML
Immunogen HIV-1 infection
Species (MHC) human (B42)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- B42 and B81 are very similar, and both can present this epitope to B42-positive effector cells – this epitope is almost certainly optimal for B81 as well – B42 and or B81 are expressed in 40-45% of Zulu and Xhosa infected individuals in South Africa, and in 14/18 B42 or B81+ individuals, the dominant gag response was to TPQDLNTML.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31/44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32/37 C-clade infected subjects.

HXB2 Location p24 (48–56)
Author Location Gag
Epitope TPQDLNTML
Immunogen HIV-1 infection
Species (MHC) human (B42)
References Goulder *et al.* 2000b

- Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]).
- HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection.

HXB2 Location p24 (48–56)
Author Location p24
Epitope TPQDLNQML
Immunogen
Species (MHC) human (B53)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective.
- HIV-2 sequence: TPYDINQML, no cross-reactivity, Gotch *et al.* [1993]

HXB2 Location p24 (48–56)
Author Location Gag (173–181 HIV-2)
Epitope TPYDINQML
Immunogen HIV-2 infection
Species (MHC) human (B53)
References Gotch *et al.* 1993

HXB2 Location p24 (48–56)
Author Location Gag (180–188 subtype A)
Epitope TPQDLNMML

Subtype A
Immunogen HIV-1 infection, in vitro stimulation or selection
Species (MHC) human (B53)
Keywords inter-clade comparisons
References Dorrell *et al.* 2001

- In vitro restimulation of CTL specific for dominant epitopes from infected individuals is possible using recombinant modified vaccinia virus Ankara (MVA) carrying A or D subtype HIV-1 Gag proteins.

HXB2 Location p24 (48–56)
Author Location p24 (180–188 subtype A consensus)
Epitope TPQDLNMML
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (B53)
Keywords inter-clade comparisons, immunodominance, TCR usage
References Dorrell *et al.* 2001

- In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays.
- This optimal epitope was identified within the 20 mer reactive peptide that carried it by homology with a B53 epitope from HIV-2, a B subtype B7 peptide that corresponds to it, as B53 is part of the B7 superfamily, and by the proline in the anchor at position 2.
- TPQDLNMML was recognized in 6/7 HLA-B53 subjects and was immunodominant in most subjects.
- TPQDLNMML was A subtype-specific with no cross-recognition of the subtype B, C, and D variant, TPQDLNTML, although the B/C/D variant bound more efficiently to B53 – position 7 show great positional variation in crystal structures of two HLA-B53 complexes, suggesting variation here might significantly alter the position of the peptide in the binding groove and thus affect TCR interactions.
- Only one subject might have had a cross-reactive response with the HIV-2 and Mamu-A*01 variant CTPYDINQML, and this subject might have been dual infected with HIV-2.

HXB2 Location p24 (48–56)
Author Location p24
Epitope TPQDLNMML
Immunogen HIV-1 infection
Species (MHC) human (B53)
Assay type Intracellular cytokine staining
Keywords immunodominance, genital and mucosal immunity
References Kaul *et al.* 2003

- Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher.
- The immunodominant response was to this epitope in the PBMC of 2/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).

HXB2 Location p24 (48–56)
Author Location p24 (180–188 IIIB)
Epitope TPQDLNTML
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope.

HXB2 Location p24 (48–56)
Author Location p24 (180–188)
Epitope TPQDLNTML
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords immunodominance
References Jin *et al.* 2000b

- This is the optimal epitope for the immunodominant response defined using a conventional approach in an HLA B7+ long-term non-progressor.
- Three additional sub-dominant HLA B7 epitopes were defined using EpiMatrix, a non-anchor based strategy for defining potential epitopes, which highlighted 2078 possible epitopes in the autologous HIV-1 derived from the study subject – this was followed by B7 anchor residue prediction which narrowed the set to 55 peptides, three of which could serve as functional CTL epitopes.

HXB2 Location p24 (48–56)
Author Location p24 (SF2)
Epitope TPQDLNTML
Epitope name TL9
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Goulder *et al.* 2001a

- Recognized by patient 9354 during chronic infection, used as a positive control in a study of the SLYNTVATL epitope.

HXB2 Location p24 (48–56)
Author Location p24 (48–56)
Epitope TPQDLNTML
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location p24 (48–56)
Author Location p24 (48–56)
Epitope TPQDLNTML
Epitope name B7-TL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.

HXB2 Location p24 (48–56)
Author Location p24
Epitope TPQDLNTML
Epitope name B7-TL9(p24)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A32, A?, B7, B14
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8+ T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT).

HXB2 Location p24 (48–56)
Author Location p24 (48–56)
Epitope TPQDLNTML
Epitope name B7-TL9 Gag
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response, but in this case the epitope did not vary.

HXB2 Location p24 (48–56)
Author Location (B consensus)
Epitope TPQDLNTML
Epitope name TL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, B07, Cw7
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope

HXB2 Location p24 (48–56)
Author Location p24 (HXB2)
Epitope TPQDLNTML
Subtype B

Immunogen in vitro stimulation or selection
Species (MHC) human (B7, Cw8, B42)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords epitope processing, vaccine antigen design, characterizing CD8+ T cell responses
References SenGupta *et al.* 2004

- Multiple HLA class I-restricted and class II-restricted T-cell epitopes were shown to be processed and presented from an exogenously added HIV-1 gag-p24 peptide complexed to a heat shock protein. T-cell recognition of the complex was shown to be inhibited by brefeldin A indicating an endoplasmic reticulum-dependent pathway.

HXB2 Location p24 (48–56)
Author Location p24 (180–188 LAI)
Epitope TPQDLNTML
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw*0802 (Cw8))
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a C*0802(Cw8) epitope.

HXB2 Location p24 (48–57)
Author Location Gag
Epitope TPQDLNMMLN
Immunogen
Species (MHC) human (B7)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay.
- TPQDLNMMLN was newly defined as an HLA-B7 epitope in this study, athough it was previously published as a B*8101 epitope.
- TPQDLNMMLN was shown to stimulate an ELISPOT response, but could not be shown to bind to HLA-B7.
- The variant TPQDLNTMLN was cross-reactive, had previously been identified as a HLA-B14 epitope, and could bind to HLA-B7.

HXB2 Location p24 (48–57)
Author Location Gag
Epitope TPQDLNMMLN
Epitope name 1309
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, A24, B07, B38, Cw07, Cw12/13
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for TPQDLNMMLN: 31%.

HXB2 Location p24 (48–57)
Author Location Gag
Epitope TPQDLNTMLN
Epitope name 1308
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7, B14)
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for TPQDLNTMLN: 31%. This epitope was not confirmed in this study, but has been reported to be a B14 epitope.

HXB2 Location p24 (49–57)
Author Location p24 (181–189 LAI)
Epitope PQDLNTMLN
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14, Cw8)
References Lubaki *et al.* 1997

- Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response.
- A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response.
- Despite this being a well defined conserved epitope, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 RAEQASQEV.
- Christian Brander notes that B14 and Cw8 are in linkage disequilibrium, and that this epitope may be Cw8.

HXB2 Location p24 (51–59)
Author Location p24
Epitope DLNTMLNTV
Immunogen HIV-1 infection
Species (MHC) chimpanzee
References Santra *et al.* 1999

- 3/4 animals displayed HIV-1 Gag-specific CTL activity.
- Effector cells from two chimpanzees were able to recognize two epitopes also recognized by human HIV-1 Gag-specific CTL (SPRTLNAWV, HLA-B7, and DLNTMLNTV, HLA-B14).

- No chimpanzee CTL were detected to the following human HIV-1 specific Gag epitopes, although they were embedded within 20mer peptides that contained a reactive epitope: ISPRTLNAW, HLA-B57; KRWIILGLNK, HLA-B27; and DRFYKTLRA, HLA-B14.

HXB2 Location p24 (51–59)
Author Location p24 (subtype A)
Epitope DLNMMLNIV
Subtype A
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B14)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T-cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T-cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T-cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location p24 (51–59)
Author Location p24
Epitope DLNMMLNIV
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls, ML1792.

HXB2 Location p24 (51–59)
Author Location p24 (183–191 LAI)
Epitope DLNTMLNTV
Epitope name G5
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location p24 (51–59)
Author Location p24 (183–191)
Epitope DLNMMLNIV
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B14)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- Variants DLNMMLNIV/DLNTMLNVV are specific for clades A/B.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B14 women, 4/4 HEPS and 3/7 HIV-1 infected women recognized this epitope, likelihood ratio 4.8, p value 0.1, and HEPS women tended to respond to DLNMMLNIV/DLNTMLNVV, while infected women tended to respond to DRF(F/W)KTLRA.
- The dominant response to this HLA allele was to this epitope for all 4/4 HEPS cases and in only one of the 3/7 HIV-1 infected women.
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.
- Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLN(M/T)LN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24.

HXB2 Location p24 (51–59)
Author Location p24
Epitope DLNMMLNIV
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002

- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.
- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location p24 (51–59)
Author Location p24 (183–191 LAI)
Epitope DLNTMLNTV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14, Cw8)
References Johnson *et al.* 1992; Nixon *et al.* 1988

- Recent evidence indicates this is a Cw8 epitope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication).

HXB2 Location p24 (51–59)
Author Location p24
Epitope DLNTMLNTV
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B14, Cw8)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A subtype consensus is identical to the B clade epitope.
- The D subtype consensus is dLNmMLNiV.
- Recent evidence indicates this is a Cw8 epitope;B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication).

HXB2 Location p24 (51–59)
Author Location p24 (183–191 LAI)
Epitope DLNTMLNTV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
Keywords review
References McMichael & Walker 1994

- Review of HIV CTL epitopes – defined by B14 motif found within a larger peptide.
- Recent evidence indicates this is a Cw8 epitope;B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication).

HXB2 Location p24 (51–59)
Author Location p24 (subtype B)
Epitope DLNTMLNTV
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (Cw8, B*1402)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among B and D clade viruses.
- The Clade A version of the epitope, DLNNMLNIV, was preferentially recognized by CTL.
- Recent evidence indicates this is a Cw8 epitope;B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication).

HXB2 Location p24 (51–60)
Author Location Gag
Epitope DLNTMLNTVG
Epitope name 1238
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A2, B14)
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for DLNTMLNTVG: 65%. This epitope was not confirmed in this study, but was previously reported to be presented by B14.

HXB2 Location p24 (51–70)
Author Location p24 (183–202 SF2)
Epitope DLNTMLNTVGGHQAAMQMLK
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A26, A30, B38.

HXB2 Location p24 (51–82)
Author Location Gag (183–214 LAI)
Epitope DLNTMLNTVGGHQAAMQMLKETINEEAAEWDR
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide

Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 2/10 reacted to this peptide.
- 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual.
- None of the 12 tested had an IgG response to this peptide.

HXB2 Location p24 (61–69)
Author Location p24 (61–69)
Epitope GHQAAMQML
Immunogen HIV-1 infection
Species (MHC) human (B*1510)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p24 (61–69)
Author Location (C consensus)
Epitope GHQAAMQML
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1510)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (61–69)
Author Location p24 (193–201 LAI)
Epitope GHQAAMQML
Subtype B
Immunogen
Species (MHC) human (B*3901)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*3901 epitope.

HXB2 Location p24 (61–69)
Author Location Gag (193–201 IIIB)
Epitope GHQAAMQML
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B38)
Assay type Chromium-release assay
References Kurane *et al.* 2003

- Three CD8+ CTL cell clones were derived from 2 HIV-1 positive asymptomatic patients, and their epitope specificities and HLA presenting proteins were defined.

HXB2 Location p24 (61–69)
Author Location p24 (193–201 LAI)
Epitope GHQAAMQML
Subtype B
Immunogen
Species (MHC) human (B39)
References Kurane & West 1998

- Optimal peptide defined by titration.

HXB2 Location p24 (61–71)
Author Location p24 (193–203 BRU)
Epitope GHQAAMQMLKE
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Claverie *et al.* 1988

- One of 4 epitopes first predicted, then shown to stimulate HLA-A2 restricted CTL line.

HXB2 Location p24 (61–71)
Author Location p24 (61–70)
Epitope GHQAAMQMLKE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 7/19 patients recognized this epitope.

HXB2 Location p24 (61–80)
Author Location p24 (193–212 SF2)
Epitope GHQAAMQMKETINEEAAEW
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A26, A30, B38.

HXB2 Location p24 (61–82)
Author Location p24 (193–214 BH10)
Epitope GHQAAMQMLKETINEEAAEWDR

Immunogen HIV-1 infection
Species (MHC) human (Bw52)
References Johnson *et al.* 1991
- Gag CTL response studied in three individuals.

HXB2 Location p24 (62–70)
Author Location p24 (194–202 LAI)
Epitope HQAAMQMLK
Subtype B
Immunogen
Species (MHC) human (B52)
References Brander & Walker 1996
- P. Goulder, pers. comm.

HXB2 Location p24 (64–80)
Author Location p24 (63–80 HXB2)
Epitope AAMQMLKETINEEAAEW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003
- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 22% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (65–72)
Author Location p24
Epitope AMQMLKET
Epitope name A9I
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Gag
Species (MHC) mouse (H-2^d)
Assay type Chromium-release assay
References Bojak *et al.* 2002b
- Codon-optimized gag gene DNA vaccines were compared to wild type by vaccination of BALB/c mice. Codon optimized DNA gave a Th1 polarized Th response, a strong antibody response that persisted from more than 20 weeks, and CTL responses, while wild-type DNA induced weak and inconsistent immune responses.

HXB2 Location p24 (65–73)
Author Location Gag (199–207)
Epitope AMQMLKETI
Epitope name p7g
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia, Sindbis *HIV component:* Gag
Species (MHC) mouse
Assay type CD8 T-cell Elispot - IFNγ
Keywords genital and mucosal immunity
References Vajdy *et al.* 2001
- Nasal, vaginal, rectal and i.m. immunization was performed with Sindbis virus expressing HIV-1 Gag (SIN-Gag), followed by intravaginal or intrarectal challenge with vaccinia virus expressing either Gag (VV-Gag) or gp160 (VV-gp160) as a control.
- Intranasal and intramuscular immunization followed by intravaginal challenge induced HIV-1 Gag specific, IFN-γ producing CD8+ T-cells in the vaginal/uteral mucosal tissue, as well as in the draining iliac lymph nodes and in the spleen, but could not protect against a VV-Gag infection of the ovaries. Local vaginal or rectal immunization, despite lower CD8+ T-cell responses, did provide protection.

HXB2 Location p24 (65–73)
Author Location Gag (Du422)
Epitope AMQMLKDTI
Subtype C
Immunogen Vaccine
Vector/Type: DNA *Strain:* C clade Du422 *HIV component:* Gag
Species (MHC) mouse
Donor MHC H-2d
Assay type Chromium-release assay
Keywords inter-clade comparisons, variant cross-recognition or cross-neutralization
References van Harmelen *et al.* 2003
- The pTHgagC DNA vaccine employed in this study expressed the gag gene derived from the South African isolate Du422, which was selected on the basis of being the natural strain most similar to the South African subtype C consensus sequence (aa distance of 1.8%).
- A E7D mutation was introduced into the epitope to match the gag subtype C sequence in the vaccine. Mice vaccinated with the gag DNA made strong CTL responses against AMQMLKDTI, boosting enhanced the response, and memory cells persisted for 15 weeks.

HXB2 Location p24 (65–73)
Author Location p24 (197–205)
Epitope AMQMLKETI?
Immunogen Vaccine

Vector/Type: protein *HIV component:* Gag *Adjuvant:* Cholera toxin (CT)
Species (MHC) mouse
Donor MHC H-2d
Assay type CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords TCR usage, genital and mucosal immunity
References Yoshizawa *et al.* 2003

- Intranasal immunization triggered CTL response in the nasal-associated lymphoid tissue (NALT), posterior cervical lymph nodes (pCLNs) and the spleen, but not in the mesenteric lymph nodes (MLNs). Rectal immunzation elicited CTL responses only in the MLNs. By immunizing mice nasally following rectal immunization, CTL responses were detected in NALT, pCLNs, spleen and MLNs. Epitope-specific CD8+ T-cells were primarily located in NALT after 6 days and in pCLNs after 2 months.
- The strongest specific lysis was induced by NALT-specific CTL clones. pCLNs derived memory CTL clones originated from NALT CTL clones, as determined by T-cell receptor Vβ usage.

HXB2 Location p24 (65–73)
Author Location Gag (199–207 HXB2)
Epitope AMQMLKETI
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2^d)
References Qiu *et al.* 1999

- Different expression vectors were tested to increase Gag expression in cell lines and create suitable vectors for DNA vaccines.
- Stable Gag expression was achieved in murine p815 cells, using a Gag gene that had mutated silent base positions that disrupt inhibitory RNA sequences which promote RNA degradation.
- Silent mutations were more effective than introduction of the D retrovirus cis-acting posttranscriptional control element (CTE) for enhancing Gag expression.
- The gag vector with silent mutations given as a vaccine to BALB/c mice gave CTL responses in splenic mononuclear cells, using peptide pulsed cells as targets.

HXB2 Location p24 (65–73)
Author Location p24 (199–207 SF2)
Epitope AMQMLKETI
Epitope name p7g
Immunogen Vaccine
Vector/Type: protein, vaccinia *Strain:* B clade SF2 *HIV component:* Gag, Gag-Pol *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse (H-2^d)
References Neidleman *et al.* 2000

- Intranasal immunization of CB6F1 (H2bxd) mice with soluble gag p55 with LT ADP-ribosyltransferase mutants (LTK63 and LTK73) from Escherichia coli as adjuvants was tested.
- Intranasal and intramucosal immunization of p55 gag protein with LTK63 or LTK72 adjuvant induced a CTL response comparable to intramuscular immunization responses.
- Oral co-administration of LTR72, with residual ADP-ribosyltransferase activity, induced systemic CTL responses, but LTK63 with no ADP-ribosyltransferase activity did not.

HXB2 Location p24 (65–73)
Author Location p24 (66–74)
Epitope AMQMLKETI
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Gag *Adjuvant:* vesicular stomatitis virus glycoprotein (VSV-G)
Species (MHC) mouse (H-2^d)
References Marsac *et al.* 2002

- BALB/c mice were injected with plasmids expressing HIV-1 Gag with or without coinjection of a plasmid expressing vesicular stomatitis virus glycoprotein (VSV-G). The combination encodes VSV-G pseudotyped Gag particles that can be taken up by cells for presentation in either the class I or class II pathways, while exogenous Gag alone can only be taken into the class II pathway.
- Vaccination with DNA expressing VSV-G pseudotyped Gag particles rather than just Gag increase Gag-specific CTL responses generally as well as the specific H-2d restricted anti-AMQMLKETI response.

HXB2 Location p24 (65–73)
Author Location Gag
Epitope ANQMLKDTI
Subtype C
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *HIV component:* Gag, Protease
Species (MHC) mouse (H-2^d)
Country India.
Assay type cytokine production, CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, cytolytic LDH release assay
Keywords inter-clade comparisons, vaccine-induced epitopes, Th1
References Chugh & Seth 2004

- A gag-protease gene construct from HIV-1 subtype C Indian strain has been shown to be successful in evoking immune responses to gag epitopes from both CD4+ and CD8+ T-cells in BALB/c mice. The immune response was of TH1 type. Recognition of seven Gag peptides carrying multiple epitopes indicates a broad-based immune response.
- A cross-clade response to the C clade epitope ANQMLKDTI was observed to the B clade version of this epitope, aNqmlkEti. 66% lysis was observed to the peptide carrying the C clade epitope, only 33% to the B clade variant.

HXB2 Location p24 (65–73)
Author Location p24 (199–207 SF2)
Epitope AMQMLKETI
Epitope name p7G
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF2 *HIV component:* Gag *Adjuvant:* DDA, DOTAP, CpG immunostimulatory sequence (ISS), MF59, PLG, urea

Species (MHC) mouse (H-2^{kd})
Keywords dendritic cells
References O'Hagan *et al.* 2002

- Intramuscular or intraperitoneal immunization of BALB/c or CB6F1 mice with urea-solubilized, emulsified, or PLG-microparticle associated p55 Gag was studied in conjunction with the adjuvant CpG. CpG did not enhance CTL immunity when combined with urea solubilized p55, but did when combined with emulsions and PLG-microparticle antigen.
- CpG shifted the Ab response towards a IgG2a, and CpG was shown to upregulate CD86 on mouse bone-marrow derived dendritic cells.

HXB2 Location p24 (65–73)
Author Location p24 (199–207 SF2)
Epitope AMQMLKETI
Subtype B
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade SF2 *HIV component:* Gag, gp120
Species (MHC) mouse (H-$2D^d$)
Assay type Chromium-release assay
Keywords epitope processing, vaccine-induced epitopes
References Doe *et al.* 1996

- Spleen cells from mice with distinct MHC types were infused into HIV vaccinated scid mice, to study the antigen presenting cells used by CTL induced in intramuscular injections. Bone marrow derived cells are used for presenation, but DNA infection is not required for priming, rather APCs can present proteins synthesized in other host cells.

HXB2 Location p24 (65–73)
Author Location p24 (199–207 SF2)
Epitope AMQMLKETI
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* Gag, Pol
Species (MHC) mouse (H-$2K^d$)
Keywords immunodominance
References Doe & Walker 1996

- Immunodominant murine CTL response to this peptide observed after immunization with vaccine VVgagpol.
- Optimal peptide was defined.

HXB2 Location p24 (65–73)
Author Location Gag (197–205)
Epitope AMQMLKETI
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *HIV component:* Gag
Species (MHC) mouse (H-$2K^d$)
References Rayevskaya & Frankel 2001

- BALB/c mice were immunized with a highly attenuated recombinant Listeria monocytogenes, Lmdaldat, that can grow only when supplemented with D-alanine, and that expresses HIV-1 HXB2 Gag.
- Parenteral immunization provided protection against systemic and mucosal challenges with a recombinant vaccinia virus expressing HIV-1 gag, and a long lasting memory CTL response against Gag in spleen, mesenteric lymph nodes, and Peyer's patches directed against the gag protein.
- Oral immunization gave protection only against mucosal virus challenge and was associated with a transient CTL response in the three lymphoid tissues examined.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.

HXB2 Location p24 (65–73)
Author Location Gag (197–205 SF2)
Epitope AMQMLKETI
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-$2K^d$)
Keywords immunodominance
References Mata *et al.* 1998

- BALB/c mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.
- This is the immunodominant CTL epitope in Gag in BALB/c mice.
- AMQMLKETI does not contain established Kd anchoring residue in position 2, tyrosine or phenylalanine, thus deviating from the typical Kd anchoring motif – the lack of the aromatic anchor residue is compensated for by interaction of the glutamine at P3 with pocket D of Kd.

HXB2 Location p24 (65–73)
Author Location Gag (HXB2)
Epitope AMQMLKETI
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia, vesicular stomatitis virus (VSV) *Strain:* B clade HXB2, B clade IIIB *HIV component:* Env, Gag
Species (MHC) mouse (H-$2K^d$)
Keywords immunodominance
References Haglund *et al.* 2002a

- Different HIV strains were used for different regions: Env IIIB, Gag HXB2.
- BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag, Env, or both, and compared to using rec Env and Gag in vaccinia virus (rVVs). The primary response was determined by cell lysis, cytokine production and tetramer staining.
- Primary CTL responses to the immunodominant Gag (AMQMLKETI) epitope peaked in 7 days for GAG-rVSV, 3% of the cells were tetramer positive, and this response was 8-fold higher than for Gag-rVV.

- Vaccinating with GagEnv-rVSV carrying both Gag and Env allowed recognition of both HIV-1 proteins, but at reduced levels compared to either Gag-rVSV or Env-rVSV alone.
- Intranasal immunization with Env-rVSV yielded CTL responses that were strong but reduced compared to an intraperitoneal route.

HXB2 Location p24 (65–73)
Author Location Gag (HXB2)
Epitope AMQMLKETI
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia, vesicular stomatitis virus (VSV) *Strain:* B clade HXB2, B clade IIIB *HIV component:* Env, Gag
Species (MHC) mouse (H-2K^{d})
Keywords immunodominance
References Haglund *et al.* 2002b

- Different HIV strains were used for different regions: Env IIIB, Gag HXB2.
- BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag or Env, or both, and retention of memory responses and recall responses were studied by tetramer staining and IFN-gamma production.
- Seven months after vaccination with Env-rVSV, 6% of the CD8+ cells were tetramer positive for the immunodominant Env epitope; these cells had a memory phenotype, CD44-Hi positive.
- Env in rec vaccinia virus (Env-rVV) elicited a strong recall response, with up to 45% to the CD8+ T-cell population tetramer positive and activated (expressing CD62L-Lo), and capable of IFN-gamma production.
- A prime with Env-rVSV and heterologous boost of Env-rVV gave remarkably high levels of memory cells, with approximately 1/3 of the CD8+ splenocytes being Env specific memory cells 150 days after the boost.
- A Gag-rVSV or EnvGag-rVSV prime and with a heterologous Gag-rVV or EnvGag-rVV boost combination gave 40% tetramer positive CD8+ cells, but the fraction of IFN-gamma producing cells was only about 25%. Still the heterologous vector prime-boost combination showed a profound benefit.
- A HIV-1 protein rVSV prime, rVV boost was a more potent combination than a vector reversal of a rVV prime and rVSV boost.

HXB2 Location p24 (65–73)
Author Location Gag
Epitope AMQMLKETI
Subtype B
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *HIV component:* Gag
Species (MHC) mouse (H-2K^d)
Donor MHC H-2d
Assay type Tetramer binding, Intracellular cytokine staining
Keywords genital and mucosal immunity
References Peters *et al.* 2003

- Intravenous, rectal, and oral vaccination of recombinant L. monocytogenes expressing HIV-1 Gag antigen were compared for their ability to stimulate a mucosal CTL response; mucosal administration of this vaccine gave strong mucosal response that was readily boosted.
- This CTL epitope is the immunodominant epitope in Gag for BALB/c mice, and was used to characterize the vaccine responses.

HXB2 Location p24 (65–73)
Author Location Gag (197–205)
Epitope AMQMLKETI
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia, Listeria monocytogenes *HIV component:* Gag, Nef
Species (MHC) mouse (H-2K^d)
Donor MHC H-2d
Assay type cytokine production, proliferation, Tetramer binding, Intracellular cytokine staining, Chromium-release assay
Keywords memory cells
References Rayevskaya *et al.* 2003

- Splenocytes derived from BALB/c mice immunized and boosted with Lmdd-gag were stimulated with gag-peptide specific antigen *in vitro*. In culture, CTL activity against this epitope reached a maximum at 9 days, then declined. Peptide restimulation gave a delayed (18 hours) but potent response, and growth was IL-2 or IL-15 dependent. Adoptive transfer of 5000 of the sorting purified cells could protect recipient BALB/c against vaccinia-gag challenge up to 3 months after transfer.

HXB2 Location p24 (65–73)
Author Location
Epitope AMQMLKETI
Epitope name A9I
Immunogen Vaccine
Vector/Type: DNA, virus-like particle (VLP), polyepitope *HIV component:* Gag, p24 Gag, V3
Species (MHC) mouse (H-2K^d)
Assay type cytokine production, Chromium-release assay
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance, vaccine antigen design
References Wild *et al.* 2004

- A codon optimized gag DNA vaccine was compared to a myristylation defective gag and p24 alone, both of which lack signals for secretion from transfected cells. Gag-derived immunogens that were secreted as VLPs and those that remained intracellular (p24) each produced strong CTL responses, and neither the size of antigen nor cellular trafficking and localization significantly influenced the strength of humoral and cellular immune activation. The formation and release of VLPs was not essential for eliciting strong CTL. BALB/c mice were given the DNA vaccine by i.m. administration of plasmid DNA for the prime and boost.

- Linking the region encoding the V3 immunodominant epitope to the gag gene did not diminish the response to the Gag p24 eptiope A9I, but did enable a response to the V3 epitope.
- Minigenes were made incorporating just one epitope, minitopes, carrying one of three murine class I eptiopes linked to the Ad2-E3 protein-derived signal peptide to allow access of the epitope to the ER. Weak induction of cellular immune resposes was observed, in contrast to the complex polyprotein.

HXB2 Location p24 (65–73)
Author Location Gag (197–205)
Epitope AMQMLKETI
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2K^d)
Country United States.
Assay type proliferation, T-cell Elispot
Keywords vaccine antigen design
References Kwak *et al.* 2004

- A recombinant vaccinia virus with HIV-1 Gag replacing the cytoplasmic domain of the B5R protein was shown to induce better primary CD4 response than recombinant vaccinia virus expressing Gag from the TK-locus; CD8 responses were less specific. When immunized BALB/c mice were challenged with a recombinant Listeria that expresses HIV-Gag, lower colony counts of Listeria were found in the liver and spleen of mice immunized with virus expressing B5R-Gag fusion protein.

HXB2 Location p24 (69–86)
Author Location Gag (201–218 LAI)
Epitope LKETINEEAAEWDRVPV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Buseyne *et al.* 1993a

- Vertical transmission of HIV ranges from 13% to 39%.
- Primary assays showed that cytotoxic activity against at least one HIV protein detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag.

HXB2 Location p24 (70–78)
Author Location
Epitope KETINEEAA
Epitope name Gag-KA9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Donor MHC A*0201 A*0217 B*0801 B*4002 Cw*0303 Cw*070
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- This epitope was newly defined in this study.
- Patient 01RCH46 was Hispanic, on HAART, and had a viral load of 21000 and CD4 count of 623 – she also recognized GELDRWEKI, p17(11-19), HLA B*4002, and TAFTIPSI, RT(128-135), HLA A*0217.
- Among HIV+ individuals who carried HLA B40, 3/5 (60%) recognized this epitope.

HXB2 Location p24 (70–78)
Author Location p24 (70–78)
Epitope KETINEEAA
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p24 (71–80)
Author Location p24 (203–212)
Epitope ETINEEAAEW
Immunogen HIV-1 infection
Species (MHC) human (A*2501)
Keywords inter-clade comparisons
References Klenerman *et al.* 1996

- The epitope was defined through direct stimulation of PBMC with 20-mer peptides.
- It is in a conserved region, ETINEEAAEW is found in most B, D, and E subtype isolates.
- DTINEEAAEW is found in A and some D subtype sequences.

HXB2 Location p24 (71–80)
Author Location p24 (203–212)
Epitope ETINEEAAEW
Immunogen HIV-1 infection
Species (MHC) human (A*2501)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*2501 epitope.

HXB2 Location p24 (71–80)
Author Location p24 (203–212)
Epitope ETINEEAAEW
Immunogen HIV-1 infection
Species (MHC) human (A*2501)
References van Baalen *et al.* 1996

- Conserved between B and D subtypes, variable in other clades; a consensus of clades A, C, F, G, and H and a peptide of HIV-2ROD over this region were not recognized by CTL recognizing the index peptide.
- C. Brander notes that this is an A*2501 epitope in the 1999 database.

HXB2 Location p24 (71–80)
Author Location p24
Epitope ETINEEAAEW
Immunogen
Species (MHC) human (A25)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective.
- HIV-2 sequence: EIINEEAAEW, no cross-reactivity van Baalen *et al.* [1996]

HXB2 Location p24 (71–80)
Author Location p24 (203–212 SF2)
Epitope ETINEEAAEW
Immunogen HIV-1 infection
Species (MHC) human (A25)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A25+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/2 group 2, and 1/3 group 3.

HXB2 Location p24 (71–80)
Author Location p24 (202–211)
Epitope ETINEEAAEW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A25)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8+ cells are found, each one constituting 30-40% of the CD8+ cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- 1/3 patients responded to this peptide with GzB producing cells, and the other two responded with IFN-gamma producing cells.

HXB2 Location p24 (71–80)
Author Location
Epitope DTINEEAAEW
Epitope name Gag-DW10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5301)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B*5301, 2/15 (13%) recognized this epitope.

HXB2 Location p24 (71–80)
Author Location
Epitope ETINEEAAEW
Epitope name Gag-EW10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5301)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B*5301, 2/15 (13%) recognized this epitope.

HXB2 Location p24 (71–80)
Author Location p24 (203–212)
Epitope DTINEEAAEW
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B53)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B53 women, 0/2 HEPS and 7/9 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in 4 of the 7/9 responsive HIV-1 infected women.

HXB2 Location p24 (71–80)
Author Location p24 (203–212 subtype A consensus)
Epitope DTINEEAAEW
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (B53)
Keywords binding affinity, inter-clade comparisons, epitope processing
References Dorrell *et al.* 2001

- In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays.
- Two of the new epitopes lacked the predicted P2 anchors, DTINEEAAEW and QATQEVKNM, and bound to B53 with high affinity, thus extending the anchor residue motif for B53 and the related B35.
- Two overlapping 20 mer peptides carry this complete epitope, but only one stimulates recognition, which could be due to different peptide processing.

- DTINEEAAEW was recognized in only 2/7 HLA-B53 subjects.
- DTINEEAAEW was not A subtype specific and there was cross-recognition although diminished, of the subtype B, C, and D variant, ETINEEAAEW.
- In one of the two subjects there was cross-recognition of the HIV-2 version of the epitope, EIINEEAADW.

HXB2 Location p24 (71–90)
Author Location p24 (203–222 SF2)
Epitope ETINEEAAEWDRVHPVVHAGP
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A2, B21.

HXB2 Location p24 (78–86)
Author Location p24 (78–86)
Epitope AEWDRLHPV
Epitope name AEW
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relative efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This was one of 8 reactive epitopes found not to vary over time.

HXB2 Location p24 (78–86)
Author Location
Epitope AEWDRVHPV
Epitope name Gag-AV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Donor MHC A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- This epitope was newly defined in this study.
- Patient 01RCH59 was Hispanic, not on HAART, and had a viral load of 5100 and CD4 count of 349 – she also recognized TERQANFL, p2p7p1p6(64-71), HLA-B*4002, and KEKGGLEGL, Nef(92-100), HLA-B*4002.
- Among HIV+ individuals who carried HLA B40, 4/5 (80%) recognized this epitope.

HXB2 Location p24 (78–86)
Author Location p24 (78–86)
Epitope AEWDRVHPV
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p24 (81–100)
Author Location p24 (81–100)
Epitope DRLHPVHAGPAAPGQMREPR
Epitope name DRL
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, immunodominance, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relative efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This epitope was not precisely defined, but was one of six epitopes found to be under positive selection for escape mutations and was completely replaced by escape variants between days 66 and 327 (drlhpvhagpIapgqmrepr).

HXB2 Location p24 (83–92)
Author Location p24 (215–223 IIIB)
Epitope VHPVHAGPIA
Immunogen HIV-1 infection
Species (MHC) human (B55)
References Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.
- LHPVHAGPVA, a variant found in HIV-1 PH136, was also recognized.
- LHPVHAGPIA, a variant found in HIV-1 RF, was also recognized.
- LHPVHAGPIT, a variant found in HIV-1 MN, was also recognized.
- LHPAQAGPIA, a variant found in HIV-1 JH3, was recognized at high peptide concentrations.

HXB2 Location p24 (84–92)
Author Location p24 (84–92)
Epitope HPVHAGPIA
Immunogen HIV-1 infection
Species (MHC) human (B*07)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p24 (84–92)
Author Location (C consensus)
Epitope HPVHAGPIA
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (84–92)
Author Location p24 (84–92)
Epitope HPVHAGPIA
Epitope name B7-HA9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection—10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 3/4 individuals had detectable responses to this epitope after STI.

HXB2 Location p24 (84–92)
Author Location p24 (84–92)
Epitope HPVHAGPVA
Epitope name B7-HA9 Gag
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The first infecting strain had the variant hpvhagpIa. The CTL response was higher to the second superinfecting variant, HPVHAGPVA.

HXB2 Location p24 (84–92)
Author Location (B consensus)
Epitope HPVHAGPVA
Epitope name HA9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, B07, Cw7
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location p24 (87–101)
Author Location Gag (219–233 LAI)
Epitope HAGPIAPGQMREPRG
Subtype B

Immunogen HIV-1 infection
Species (MHC) human
References Buseyne *et al.* 1993a

- Vertical transmission of HIV ranges from 13% to 39%.
- Primary assays showed that cytotoxic activity against at least one HIV protein detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag.

HXB2 Location p24 (87–101)
Author Location p24 (219–233 BRU)
Epitope HAGPIAPGQMREPRG
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Claverie *et al.* 1988

- One of 4 epitopes predicted then shown to stimulate HLA-A2 restricted CTL line.

HXB2 Location p24 (87–101)
Author Location p24 (87–101)
Epitope HAGPIAPGQMREPRG
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 19 patients recognized this epitope.

HXB2 Location p24 (91–110)
Author Location p24 (223–242 SF2)
Epitope IAPGQMREPRGSDIAGTTST
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A2, A24, B13, B35.

HXB2 Location p24 (101–120)
Author Location p24 (233–252 SF2)
Epitope GSDIAGTTSTLQEQIGWMTN
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A26, A30, B38.

HXB2 Location p24 (107–115)
Author Location Gag (239–247 SF2)
Epitope TTSTLQEQI
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2K^{d})
References Mata *et al.* 1998

- BALB/c mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.

HXB2 Location p24 (108–117)
Author Location
Epitope TSTLQRQIGW
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls (ML1250).

HXB2 Location p24 (108–117)
Author Location
Epitope TSTLQEQIGW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords rate of progression, immunodominance
References Migueles & Connors 2001

- HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.

HXB2 Location p24 (108–117)
Author Location
Epitope TSTLQEQIGW
Subtype B
Immunogen HIV-1 infection

Species (MHC) human (B*5701)
Keywords rate of progression, immunodominance
References Migueles & Connors 2001

- CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.
- CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia.
- The HLA-A*0201 SLYNTVATL epitope response was not as strong in individuals that carried both A2, B57.

HXB2 Location p24 (108–117)
Author Location
Epitope TSTLQEQIGN
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Assay type Intracellular cytokine staining, Flow cytometric CTL assay
Keywords rate of progression, escape
References Migueles *et al.* 2003

- cDNA Gag sequences from a set of 17 HLA-B*5701+ progressors and 10 LTNPs were obtained, and the variation in four p24 B*5701 epitopes examined. Sequence variants were more common ($p < 0.01$) in the epitopes in the progressors (median 3, range 1-7) than LTNPs (median 2, range 0-4).
- In general, use of the autologous protein in a target cell did not diminish the overall CD8+ T-cell responses.

HXB2 Location p24 (108–117)
Author Location p24 (241–250 LAI)
Epitope TSTVEEQQIW
Subtype B
Immunogen HIV-2 infection
Species (MHC) human (B*5801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5801 epitope.

HXB2 Location p24 (108–117)
Author Location p24 (240–249 LAI)
Epitope TSTLQEQIGW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5801 epitope.

HXB2 Location p24 (108–117)
Author Location (C consensus)
Epitope TSTLQEQIAW
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*5801, B57)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (108–117)
Author Location p24 (233–252)
Epitope TSTLQEQIGW
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Bernard *et al.* 1998

- This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population.
- No direct CTL were found in any of the six INHIs, but above background CTLp activity was found in 3/6 INHIs.
- Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XSXXXXXXXW is a B57 binding motif, and CTL activity against TSTLQEQIGW has been found in two other B57 long-term non-progressors.

HXB2 Location p24 (108–117)
Author Location Gag (SF2)
Epitope TSTLQEQIGW
Epitope name TW10
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, acute infection
References Goulder *et al.* 2001a

- Dominant epitope in acute infection in patient PI004, who did not receive any antiviral therapy.
- 1-2 months post seroconversion, subject PI004 displayed a significant decrease in TW10 peptide recognition, followed by an increased CTL response against epitope SL9, SLYNTVATL and other epitopes.
- Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.

HXB2 Location p24 (108–117)
Author Location p24 (108–117)
Epitope TSTLQEQIGW
Epitope name TST
Immunogen HIV-1 infection
Species (MHC) human (B57)

Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- None of the 8 study subjects recognized this epitope but none were HLA B57+.

HXB2 Location p24 (108–117)
Author Location p24 (108–117)
Epitope TSTLQEQIGW
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (108–117)
Author Location p24
Epitope TSTLQEQIGW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002

- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.
- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location p24 (108–117)
Author Location p24
Epitope TSTLQEQIGW
Epitope name TST
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFN? Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location p24 (108–117)
Author Location Gag (147–155)
Epitope TSTLQEQIAW
Epitope name TW10
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B57)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords epitope processing, escape
References Draenert *et al.* 2004b

- 174 people who have C clade infections were studied – those who carried B57 have 2 positions in which their HIV Gag consensus is different than the C consensus. One mutation is within this epitope, TW10, at position 3, and is believed to be an anchor residue. The other is in the N-terminal flanking position of the epitope ISPRTLNAW and is thought to impact processing.

HXB2 Location p24 (108–117)
Author Location Gag (240–249)
Epitope TSTLQEQIAW
Epitope name TW10
Subtype B, C
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords escape, reversion, viral fitness
References Leslie *et al.* 2004

- TSTLQEQIAW (the consensus form in the C clade) responses dominate the immune response in HLA-B57 individuals, and this epitope is also recognized in HLA-B5801 individuals. TSnLQEQIAW is shown to be an escape mutant correlated with HLA-B57 and HLA-B5801 alleles. The variant can be transmitted to HLA-B57/B5801 negative individuals, but reverts to wild-type in those. A second escape mutation within the epitope is, however, maintained after transmission; TSNLQEQIGW is the most common from of the epitope in the B clade, and a G substitution to some other amino acid, often A, was frequently noted in B57+ individuals; transmission of these variants persist in the new host.

HXB2 Location p24 (108–117)
Author Location p24 (108–117)
Epitope TSTLQEQIGW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 7 patients recognized this epitope.

HXB2 Location p24 (108–117)

Author Location (B consensus)
Epitope TSTLQEQIGW
Epitope name TW10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country United Kingdom.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords immunodominance, escape, characterizing CD8+ T cell responses
References Allen *et al.* 2004

- This study characterizes an escape mutation in a C-terminal flanking residue of the HLA-A3 gag p17 KK9 epitope that inhibits processing, and is embedded in the overlapping HLA-A3 RK9 epitope.
- The immune response was tracked in subject AC-38. The acute immunodominant response was to the B57 TW10 epitope; this response declined following viral escape (tsNlqeqigw) by day 64. The p17 KK9 and RK9 became immunodominant, but then declined and as the escape mutation arose. TW10 is one of three other strong responses and that persisted, along with one sub-dominant response.

HXB2 Location p24 (108–117)
Author Location p24
Epitope TSTLQEQIGW
Epitope name TW10
Immunogen HIV-1 infection
Species (MHC) human (B57, B*5801)
Keywords review, rate of progression, immunodominance, escape, acute infection, reversion, viral fitness
References Goulder & Watkins 2004

- This paper is a review of the role of CTL in HIV infection, and it uses the TW10 epitope as an example. HLA B*57 and B*5801 both can present this epitope, and are associated with successful containment of HIV infection. The early response to TW10 is immunodominant, and often followed by rapid escape due to the T->N substitution, tsNlqeqigw. Some long term survivors do not carry the escape form, possibly because the CTL response to this epitope is able to suppress viremia. Others do carry the N escape form, and presumably control viremia due to viral attenuation; in support of this the N rapidly back mutates to T in a new host, so there is likely to be a high fitness cost. In contrast, the epitope sometimes contains a G->A substitution at position 9, and the A can persist in a new host after transmission.

HXB2 Location p24 (108–117)
Author Location p24 (235–243)
Epitope TSTLQEQIGW
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B57, B58)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- TSTLQEQIGW cross reacts with both A and B clades.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location p24 (108–117)
Author Location p24 (108–117)
Epitope TSTLQEQIGW
Immunogen HIV-1 infection
Species (MHC) human (B57, B58)
Donor MHC A1, A26, B35, B57, Cw4, Cw0601; A1, A30, B42, B52, Cw7, Cw17; A1, A*0201, B44, B57, Cw5, Cw6
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins, cross-presentation by different HLA
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- This epitope was recognized in three of the acutely infected individuals and was presented by both HLA-B57 and B58.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.

HXB2 Location p24 (108–117)
Author Location Gag (240–249)
Epitope TSTLQEQIGW
Epitope name gag 240-9
Immunogen HIV-1 infection, HIV-2 infection
Species (MHC) human (B57, B58)
Country Gambia.
Assay type Intracellular cytokine staining
Keywords escape, TCR usage, variant cross-recognition or cross-neutralization, characterizing CD8+ T cell responses
References Lopes *et al.* 2003

- CD8+ T cells from HIV-2 infected patients had more polyclonal TCR responses than HIV-1 infected patients, who tended to have oligoclonal responses. This results in limited plasticity of T cell responses to amino acid substitutions within epitopes in HIV-1 infections. HIV-2-specific CD8+ T-cells showed a more

diverse TCR usage associated with enhanced CD8 expansion and IFN-gamma production on cross-recognition of variant epitopes.
- This peptide was recognized by a CD8+ T-cell clonotype with Vbeta5.1 usage in one HIV-1 infected patient, and all HIV-1 patients had narrow TCR usage, while HIV-2 patients used multiple TCR Vbeta chains. The HIV-2 variant of this peptide is: tstVEeqiQw. 5/6 HIV-2 infected individuals could recognize both the HIV-1 and HIV-2 peptides, while 0/5 HIV-1 infected patients that could react with the HIV-1 peptide could also react with the HIV-2 peptide.

HXB2 Location p24 (108–117)
Author Location p24 (241–250)
Epitope TSTVEEQQIW
Immunogen HIV-2 infection
Species (MHC) human (B58)
References Bertoletti 1998
- HIV-2 epitope defined from an infection in Gambia, Bertoletti, pers. comm.
- All HIV-2 sequences from the database are TSTVEEQIQW in this region, not TSTVEEQQW as in the paper.

HXB2 Location p24 (108–117)
Author Location p24
Epitope TSTLQEQIGW
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B58)
References Rowland-Jones *et al.* 1999
- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective.
- HIV-2 sequence: TSTVEEQIQW, CTL are cross-reactive, Bertoletti *et al.* [1998]

HXB2 Location p24 (108–117)
Author Location p24 (240–249)
Epitope TSTLQEQIGW
Immunogen HIV-2 infection
Species (MHC) human (B58)
Keywords inter-clade comparisons, rate of progression, immunodominance
References Bertoletti *et al.* 1998
- CTL responses in HLA-B*5801 positive HIV-2 infected individuals have a dominant response to Gag and tolerate extensive substitution, thus HLA-B*5801+ individuals may have an enhanced potential for cross-protection between HIV-1 and HIV-2.
- This can be an immunodominant epitope in HLA-B57 and B*5801 infected individuals, and is associated with long-term non-progression Goulder *et al.* [1996b]
- HIV-2 sequence: HIV-2 ROD has the epitope sequence TSTVEEQIQW, and the CTL from a person infected with HIV-2 was cross-reactive with HIV-1 epitopes.
- The epitope is TSTLQEQIGW in HIV-1 B clade, and TSTVEEQIQW in HIV-2 ROD.
- HLA B*5801 and B35 may preferentially select HIV-1 and HIV-2 cross-reactive epitopes.

HXB2 Location p24 (108–117)
Author Location p24 (240–249 SF2)
Epitope TSTLQEQIGW
Immunogen HIV-1 infection
Species (MHC) human (B58)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b
- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B58+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/0 group 3.

HXB2 Location p24 (108–117)
Author Location p24 (108–117)
Epitope TSTLQEQIGW
Epitope name TW10
Immunogen HIV-1 infection
Species (MHC) human (B58)
Keywords acute infection
References Goulder *et al.* 2001c
- Responses to this dominant A3-restricted Gag epitope are present during the time of decreasing viral load in acute infection.
- Mutations in this epitope were observed in autologous clones of subjects who were B58-positive with a higher frequency than those who were B58-negative (P = 0.02)
- These mutations are being sexually transmitted in adult infections.

HXB2 Location p24 (108–118)
Author Location p24 (240–249 LAI)
Epitope TSTLQEQIGWF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*57, B*5801)
Keywords rate of progression
References Goulder *et al.* 1996b
- Response to this epitope was found in 4 slow progressing HLA-B*57 individuals, in 2 it was dominant or very strong.
- For one donor (from Zimbabwe) this was defined as the optimal peptide.
- This epitope can be presented in the context of the closely related HLA molecules B*5801 and B*57.

HXB2 Location p24 (108–118)

Author Location p24 (240–249 LAI)
Epitope TSTLQEQIGWF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5701 epitope.

HXB2 Location p24 (108–118)
Author Location
Epitope TSTLQEQIGWF
Epitope name Gag-TF11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B57, 2/5 (40%) recognized this epitope.

HXB2 Location p24 (109–117)
Author Location Gag (241–249 LAI)
Epitope STLQEQIGW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701, B*5801)
Keywords rate of progression
References Klein *et al.* 1998

- B57 has been associated with long-term non-progression in the Amsterdam cohort.
- The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag.

HXB2 Location p24 (109–117)
Author Location
Epitope STLQEQIGW
Epitope name Gag-SW9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B57, 1/5 (20%) recognized this epitope.
- Among HIV+ individuals who carried HLA B58, 1/4 (25%) recognized this epitope.

HXB2 Location p24 (110–118)
Author Location Gag (242–)
Epitope TLQEQIGWM
Epitope name Gag242
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was an intermediate A2 binder that did not induce CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.

HXB2 Location p24 (118–126)
Author Location Gag
Epitope MTSNPPIPV
Epitope name Gag 271
Subtype M
Immunogen Vaccine, in vitro stimulation or selection *Vector/Type:* DNA, peptide *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, mouse (A*0201)
Assay type cytokine production, T-cell Elispot
Keywords inter-clade comparisons, computational epitope prediction, escape, TCR usage, variant cross-recognition or cross-neutralization
References McKinney *et al.* 2004

- This study examined variant recognition of epitopes presented by A*0201 and A*1101. Numerous amino acid substitutions can be introduced into epitopes without disrupting their recognition by CTLs, although epitopes with multiple substitutions were less recognized. An algorithm was constructed for prediction of epitopes capable of inducing responses to a great number of variant epitopes.
- MTSNPPIPV form is most common in subtype C while MTnNPPIPV form is mostly found in subtype B.
- A total of 14 variant forms of Gag 271 were identified. Immunization with MTSNPPIPV form induced CTLs recognizing 11 of the variant forms while MTnNPPIPV form induced CTLs recognizing only 3 of the epitope variants.

HXB2 Location p24 (118–126)
Author Location Gag (282–290)
Epitope MTNNPPIPV
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

HXB2 Location p24 (121–135)

Author Location p24 (121–135 HXB2)
Epitope NPPIPVGEIYKRWII
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (121–135)
Author Location p24 (253–267)
Epitope NPPIPVGEIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Gotch *et al.* 1990

- High frequency of memory and effector Gag-specific CTL.

HXB2 Location p24 (121–135)
Author Location p24 (255–274 SF2)
Epitope NPPIPVGEIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords review, immunodominance, escape
References Goulder *et al.* 1997a; Phillips *et al.* 1991

- Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time.
- Goulder *et al.* [1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients.

HXB2 Location p24 (121–135)
Author Location p24 (121–135)
Epitope NPPIPVGEIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (121–140)
Author Location p24 (253–272)
Epitope NPPIPVGEIYKRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location p24 (121–140)
Author Location p24 (253–272 SF2)
Epitope NPPIPVGEIYKRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- Two of these 12 had CTL response to this peptide.
- The responding subjects were HLA-A2, A3, B8, B62, and HLA-A1, B8, B18.

HXB2 Location p24 (121–140)
Author Location p24 (253–272 SF2)
Epitope NPPIPGEIKRWIILGNIK
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location p24 (121–140)
Author Location p24 (255–274 SF2)
Epitope NPPIPVGEIYKRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human
References van Baalen *et al.* 1993

- Gag CTL epitope precursor frequencies were estimated and peptide mapping was performed.

HXB2 Location p24 (121–142)
Author Location p24 (253–274 BH10)
Epitope NPPIPVGEIYKRWIILGLNKIV
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Johnson *et al.* 1991

- Gag CTL response studied in three individuals.

HXB2 Location p24 (121–152)
Author Location Gag (183–214 LAI)
Epitope NPPIPVGEIYKRWIILGLNKIVRMYSPTSILD
Subtype B
Immunogen Vaccine

Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000
- Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 9/10 reacted to this peptide.
- 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in four vaccinees.
- All of the 12 tested had an IgG response to this peptide.

HXB2 Location p24 (121–152)
Author Location Gag
Epitope NPPIPVGEIYKRWIILGLNKIVRMYSPTSILD
Immunogen HIV-1 infection, Vaccine
Vector/Type: lipopeptide *HIV component:* Gag
Species (MHC) human (A*0201)
References Seth *et al.* 2000
- Immunization of 2/4 HIV seropositive HLA selected individuals with a 32 amino acid Gag lipopeptide that contains CTL epitopes restricted by HLA A33, B8, B27, B35, and Bw62 gave a transient increase in peptide-specific bulk CTL response, but they did not decrease plasma viral load.
- Placebo and HLA mis-matched controls showed no change in CTL.
- The responders carried HLA Bw62 and B35 – the two HLA-matched that did not respond carried B35 and B8.

HXB2 Location p24 (122–130)
Author Location p24
Epitope PPIPVGDIH
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c
- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls, ML887.

HXB2 Location p24 (122–130)
Author Location p24 (260–268 LAI)
Epitope PPIPVGDIY
Subtype B
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*3501 epitope.

HXB2 Location p24 (122–130)
Author Location p24 (245–253 HIV-2)
Epitope NPVPVGNIY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Rowland-Jones *et al.* 1995

HXB2 Location p24 (122–130)
Author Location p24 (245–253 HIV-2)
Epitope NPVPVGNIY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*3501 epitope.

HXB2 Location p24 (122–130)
Author Location p24 (260–268 LAI)
Epitope PPIPVGDIY
Subtype B
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human (B35)
References Rowland-Jones *et al.* 1995
- Defined as minimal peptide by titration curve, PPIPVGEIY and HIV-2 form NPVPVGNIY are also recognized.

HXB2 Location p24 (122–130)
Author Location p24 (260–268 LAI)
Epitope PPIPVGDIY
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (B35)
References Lalvani *et al.* 1997
- A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers.
- This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors.

HXB2 Location p24 (122–130)
Author Location p24 (260–268 LAI)
Epitope PPIPVGDIY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords review
References McMichael & Walker 1994
- Review of HIV CTL epitopes.

HXB2 Location p24 (122–130)
Author Location p24 (subtype B)
Epitope PPIPVGEIY
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B35)

Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among B and D clade viruses.
- The Clade A version of the epitope, PPIPVGDIY, was preferentially recognized by CTL.

HXB2 Location p24 (122–130)
Author Location
Epitope PPIPVGEIY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers—high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location p24 (122–130)
Author Location p24
Epitope PPIPVGDIY
Immunogen
Species (MHC) human (B35)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective.
- HIV-2 version of this epitope is not conserved: NPVPVGNIY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also Rowland-Jones *et al.* [1995]

HXB2 Location p24 (122–130)
Author Location p24 (260–268)
Epitope PPIPVGDIY
Epitope name PPI
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- One of two HLA B35+ among the eight study subjects recognized this epitope.
- Patient SC15 (HLA A1/68, B8/35, Bw4/6, Cw4/0704) was given acute and sustained therapy and recognized epitopes PPIPVGDIY and VPLRPMTY during 331 days of HAART treatment.

HXB2 Location p24 (122–130)
Author Location p24 (122–130)
Epitope PPIPVGDIY
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (122–130)
Author Location p24 (254–262 SF2)
Epitope PPIPVGDIY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3.

HXB2 Location p24 (122–130)
Author Location p24 (260–268)
Epitope PPIPVGDIY

Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B35)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B35 women, 1/3 HEPS and 3/4 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in the 1/3 HEPS case and in the all 3/4 responsive HIV-1 infected women.
- Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion.

HXB2 Location p24 (122–130)
Author Location
Epitope PPIPVGDIY
Epitope name Gag-PY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B35, 2/21 (10%) recognized this epitope.
- Among HIV+ individuals who carried HLA B*5301, 0/11 (0%) recognized this epitope.

HXB2 Location p24 (122–130)
Author Location p24
Epitope PPIPVGEIY
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human (B35)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location p24 (122–130)
Author Location p24 (260–268)
Epitope PPIPVGDIY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- None of three patients responded to this peptide with GzB producing cells and one of the patients responded with IFN-gamma producing cells.

HXB2 Location p24 (122–130)
Author Location Gag
Epitope PPIPVGEIY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- No one, 0/3 HLA B35+ infection-resistant men, and 0/5 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location p24 (122–130)
Author Location p24 (122–130)
Epitope PPIPVGDIY
Immunogen HIV-1 infection

Species (MHC) human (B35)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 4/9 patients recognized this epitope.

HXB2 Location p24 (122–130)
Author Location (C consensus)
Epitope PPVPVGDIY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (122–130)
Author Location Gag (254–262)
Epitope PPIPVGEIY
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B7 supertype)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location p24 (124–138)
Author Location p24 (256–270 LAI)
Epitope IPVGEIYKRWIILGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Buseyne *et al.* 1993b

- Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.

HXB2 Location p24 (124–138)
Author Location Gag (256–270 LAI)
Epitope IPVGEIYKRWIILGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Buseyne *et al.* 1993a

- Vertical transmission of HIV ranges from 13% to 39%.
- Primary assays showed that cytotoxic activity against at least one HIV protein was detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Two children, EM16 (CDC P2A+D2) and EM18 (CDC P2A), had a CTL response to this epitope, and it was shown to be presented by B8 in EM18.

HXB2 Location p24 (126–140)
Author Location p24 (126–140 HXB2)
Epitope VGEIYKRWIIGLNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (127–135)
Author Location p24 (259–267 SF2)
Epitope GDIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
References McAdam *et al.* 1998
- GDIYKRWII specific CTL clone also recognized GEIYKRWII.

HXB2 Location p24 (127–135)
Author Location p24 (261–269)
Epitope GEIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Sutton *et al.* 1993
- Predicted epitope based on B8-binding motifs, from larger peptide NPPIPVGEIYKRWII.

HXB2 Location p24 (127–135)
Author Location p24 (259–267)
Epitope GEIYKRWII
Immunogen in vitro stimulation or selection
Species (MHC) human (B8)
Keywords dendritic cells
References Zarling *et al.* 1999
- This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses.
- Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA.
- A weak response to KLTPLCVSL was stimulated using macrophages as the APC.
- No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.

HXB2 Location p24 (127–135)
Author Location p24 (259–267 LAI)
Epitope GEIYKRWII
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Klenerman *et al.* 1994
- Naturally occurring variant GDIYKRWII may act as antagonist.

HXB2 Location p24 (127–135)
Author Location p24 (259–267)
Epitope GEIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords immunodominance
References Betts *et al.* 2000
- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope as well as seven others.

HXB2 Location p24 (127–135)
Author Location p24 (259–267)
Epitope GEIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords dynamics, escape
References Nowak *et al.* 1995
- Longitudinal study of CTL response and study of immune escape – GDIYKRWII could also stimulate CTL, reactivity fluctuated.

HXB2 Location p24 (127–135)
Author Location p24 (259–267)
Epitope GEIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
References McAdam *et al.* 1995
- Equivalent sequence GDIYKRWII also recognized by CTL from some donors.

HXB2 Location p24 (127–135)
Author Location p24 (259–267)
Epitope GEIYKRWII
Epitope name GEI
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, escape, acute infection
References Oxenius *et al.* 2000
- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- Six of the 7/8 study subjects that were HLA B8 recognized this epitope.
- Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responsiveness against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII peptides – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones.
- Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQGYFPDWQNY, and GEIYKRWII and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent.

- Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197.
- Patient SC10(HLA A1/3, B8/35, DR1/8, DQ 4/5) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL and a response to GEIYKRWII through day 1088.
- Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy.
- Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640 had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy.

HXB2 Location p24 (127–135)
Author Location p24 (259–267 SF2)
Epitope GEIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 2/3 group 1, 2/3 group 2, and 2/2 group 3.

HXB2 Location p24 (127–135)
Author Location p24
Epitope GEIYKRWII
Epitope name GEI
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location p24 (127–135)
Author Location p24
Epitope GEIYKRWII
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human (B8)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location p24 (127–135)
Author Location Gag (259–267)
Epitope GEIYKRWII
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B8)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the most frequently recognized of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location p24 (127–135)
Author Location p24 (259–267)
Epitope GEIYKRWII
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- None of three patients responded to this peptide with GzB producing cells and one of the patients responded with IFN-gamma producing cells.

HXB2 Location p24 (127–136)
Author Location
Epitope GEIYKRWIIL
Epitope name Gag-GL10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Donor MHC A*0101 A*0301 B*0801 B*5802 Cw*0602 Cw*0701
Assay type Chromium-release assay
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Among HIV+ individuals who carried HLA B08, 3/6 (50%) recognized this epitope.

HXB2 Location p24 (128–135)
Author Location p24 (260–267 LAI)
Epitope EIYKRWII
Subtype B
Immunogen
Species (MHC) human (B*0801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0801 epitope.

HXB2 Location p24 (128–135)
Author Location (C consensus)
Epitope DIYKRWII
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (128–135)
Author Location p24 (260–267 LAI)
Epitope EIYKRWII
Subtype B
Immunogen
Species (MHC) human (B8)
References Goulder *et al.* 1997g

- Defined in a study of the B8 binding motif.

HXB2 Location p24 (128–135)
Author Location p24 (SF2)
Epitope EIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in an HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location p24 (128–135)
Author Location p24 (C consensus)
Epitope DIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in an HIV+ South African – this epitope did not fall within the five most recognized peptides in the study.

- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location p24 (128–135)
Author Location p24 (SF2)
Epitope EIYKRWII
Epitope name EI8
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Goulder *et al.* 2001a

- This peptide elicited a weak CTL response during acute HIV-1 infection in patient PI004.
- Three CTL responses to epitopes, TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.

HXB2 Location p24 (128–135)
Author Location p24
Epitope EIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords rate of progression
References Kostense *et al.* 2001

- HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load.
- Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional.
- In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival.
- 4/13 patients that reacted with EIYKRWII displayed epitope mutations in a minority of sequences, which did not correlate with disease progression or viral load – these mutations were: Patient 156 (KIYKRWMI), Patient 36 (EIYKRRII), Patient 656 (KIYKRWII, EIYERWMI), and Patient 159 (EIYKRWVI).
- Stimulation with HLA-B8 p24 and Nef epitopes significantly increased Nef-specific T-cell numbers in 2 patients (748 and 1113)
- There were more functional IFN-gamma producing Nef-specific T-cells within the T-cell population than there were active p24 Gag-specific T-cells.

HXB2 Location p24 (128–135)
Author Location p24 (259–267)
Epitope DIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Appay *et al.* 2000

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

HXB2 Location p24 (128–135)
Author Location p24 (128–135)
Epitope EIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Day *et al.* 2001

- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.

HXB2 Location p24 (128–135)
Author Location Gag
Epitope EIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Goulder *et al.* 2000b

- Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA])
- HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection.

HXB2 Location p24 (128–135)
Author Location p24
Epitope DIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A2, A11, B8, B60, Bw6
Keywords HAART, ART
References Appay *et al.* 2002

- Four HIV patients with prolonged clinically successful antiviral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

HXB2 Location p24 (128–135)
Author Location Gag (260–267 IIIB)
Epitope EIYKRWII
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)

Assay type Chromium-release assay
References Kurane *et al.* 2003

- Three CD8+ CTL cell clones were derived from 2 HIV-1 positive asymptomatic patients, and their epitope specificities and HLA presenting proteins were defined.

HXB2 Location p24 (128–135)
Author Location Gag (B con)
Epitope EIYKRWII
Epitope name E18
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords variant cross-recognition or cross-neutralization
References Draenert *et al.* 2004c

- CD8 T-cell responses that persisted in individuals with advanced disease were studied; most of the optimal epitopes defined were recognized with intermediate to high avidity. On average 13 (range, 2-39) epitopic regons were targeted in an average of 6 proteins (range, 1-8). HAART resulted in decrease in antigen and reduction in gamma IFN EliSpot responses, suggesting active responses to autologous virus. Limited or no mutations within most viral epitopes suggest that persistent CTL through late disease do not exert strong immune selection pressure, yet the Elispot assays show robust responses, suggesting to the authors that gamma IFN based screening methods may not reveal functional CD8+ T-cell impairment in patients with AIDS.
- Three subjects recognized this epitope, with intermediate functional avidity. Autologous sequence revealed one substitution, Diyrkwil, in one of the three; this version of the epitope also had intermediate functional avidity with the donor's cells.

HXB2 Location p24 (128–135)
Author Location Gag
Epitope EIYKRWII
Immunogen HIV-1 infection
Species (MHC) human (B8)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- 3/9 HLA B8+ infection-resistant men, compared to 1/3 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location p24 (128–135)
Author Location (B consensus)
Epitope EIYKRWII
Epitope name EI8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A02, A03, B08, B62, Cw7, Cw10; A11, A29, B08, B44, Cw4, Cw7; A25, A32, B08, B14, Cw7, Cw8; A01, A03, B08, B14, Cw7, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found
- 4/9 individuals recognized this epitope, presented by HLA-B8.

HXB2 Location p24 (128–135)
Author Location p24
Epitope DIYKRWII
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Country United Kingdom.
Assay type Tetramer binding, T-cell Elispot, Intracellular cytokine staining
Keywords rate of progression, acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Papagno *et al.* 2004

- Acute HIV-1 infection induces massive activation of HIV-specific and non-HIV-specific CD8+ T-cells resulting in differentiation of these cells. High differentiation of CD8+ T-cells is correlated with disease progression. Differentiation is a natural process but it can be driven by elevated immune activation, such as in HIV infection.

HXB2 Location p24 (128–136)
Author Location Gag (260–268 SUMA)
Epitope EIYKRWIIL
Epitope name Gag EIL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location p24 (128–136)
Author Location Gag (260–268)
Epitope EIYKRWIIL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A2)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the most frequently recognized of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location p24 (129–136)
Author Location p24 (263–270 SF2)
Epitope IYKRWIIL
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 1/4 HIV-1 + people tested.
- IYKRWIIL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location p24 (129–138)
Author Location p24 (263–272 SF2)
Epitope IYKRWIILGL
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 1/4 HIV-1 + people tested.
- IYKRWIILGL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location p24 (129–138)
Author Location Gag (261–270)
Epitope IYKRWIILGL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A24)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location p24 (129–138)
Author Location p24 (263–272)
Epitope IYKRWIILGL
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was B27 and responded to IYKRWIILGL.

HXB2 Location p24 (129–148)
Author Location Gag (261–280)
Epitope IYKLWIILGLNKIVRMYSPT
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27, B62)
Donor MHC A3, A31, B27, B38; A24, B27, B62
Assay type Chromium-release assay

Keywords genital and mucosal immunity
References Musey *et al.* 2003

- CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, were primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments.
- CD8+ T cell clones directed at this epitope were derived from blood and rectum of one individual, and blood and semen of another. Both individuals are HLA-B27 positive, and within the peptide there is a B27 epitope that was recognied in the blood and rectum of the first patient, and in the blood of the second. A HLA-B62 epitope is also recognized in this peptide in the second individual, and the CD8+ T cells clones from both the blood and semen recognized this epitope.

HXB2 Location p24 (130–148)
Author Location p24 (265–280 BRU)
Epitope YKRWIILGLNKIVRMYSPT
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Dadaglio *et al.* 1991

- Used as a positive control for HLA specificity.

HXB2 Location p24 (131–139)
Author Location Gag (265–273)
Epitope KRWIILGLN
Immunogen HIV-1 infection
Species (MHC) chimpanzee (Patr-B*03)
References Balla-Jhagjhoorsingh *et al.* 1999b

- Certain HLA-alleles have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57.
- Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS.
- CTL responses were studied in two HIV-1 infected chimpanzees that have strong CTL responses, and they were found to respond to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57.
- The human HLA protein which presents this Patr-B*03 epitope is HLA B*2705 but the amino acid sequences in the binding pockets of HLA-B*2705 and Patr-B*03 are distinctive.

HXB2 Location p24 (131–140)
Author Location Gag (263–272 LAI)
Epitope KRWILLGLNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Buseyne *et al.* 1993a

- Vertical transmission of HIV ranges from 13% to 39%.
- Primary assays showed that cytotoxic activity against at least one HIV protein was detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B*27)
Keywords HAART, ART
References Huang *et al.* 2000

- The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed.
- Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT.
- In 3/3 HLA A*02, B*27 individuals, the dominant response in gag measured by both gamma IFN production and T cell lysis was to the B27 epitope, KRWIILLGLNK, not the A2 SLYNTVATL epitope.

HXB2 Location p24 (131–140)
Author Location p24 (263–272 SF2)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B*27)
References McAdam *et al.* 1998

- Epitope invariant across clades A, B, C, and D.

HXB2 Location p24 (131–140)
Author Location p24 (260–269 HIV-2)
Epitope RRWIQLGLQK
Immunogen
Species (MHC) human (B*2703)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*2703 epitope.

HXB2 Location p24 (131–140)
Author Location p24
Epitope KRWIILGGLNK
Immunogen HIV-1 infection
Species (MHC) human (B*2705)
Keywords dynamics, acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- Tetramers with peptide variants KRWIILGGLNK and KRWIIMGGLNK were used – CTL from most B27 donors recognize both variants, although one of the three subjects recognized only KRWIILGGLNK.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong strong response to SLYNTVATL.

- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location p24 (131–140)
Author Location p24 (263–272 LAI)
Epitope KRWIILGLNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*2705)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*2705 epitope.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B*2705)
Keywords escape
References Kelleher *et al.* 2001b

- A mutation in 4/5 B*2705 patients had substitution to lysine (K) at HIV-1 gag residue 264 (R264K), in three the change occurred late in infection – in one patient a substitution of glycine at HIV-1 gag residue 264 (R264G) was detected – these substitutions reduce binding to B27.
- The R264K mutations were associated with a L268M mutation that may be compensatory, and R264G occurred in conjunction with E260D.
- Positions 260, 264, and 268 all lie along one aspect of helix seven of the capsid protein, a region that is important for capsid self-association and assembly.
- R264G and R264K escape mutation outgrowth occurred in conjunction with high viral loads.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIIMGLNK
Immunogen HIV-1 infection
Species (MHC) human (B*2705)
References Appay *et al.* 2000

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

HXB2 Location p24 (131–140)
Author Location p24
Epitope KRWIILGLNK
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human (B*2705)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location p24 (131–140)
Author Location p24 (263–272 LAI)
Epitope KRWIILGLNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*2705, B27)
Keywords review, rate of progression, immunodominance, escape
References Goulder *et al.* 1997c; Goulder *et al.* 1997a

- HLA-B*2705 is associated with slow HIV disease progression.
- 11/11 HLA-B*2705 donors make a response to this epitope, usually an immunodominant response.
- This is a highly conserved epitope.
- The HLA-B*2705 binding motif includes R at position 2, and L in the C-term position.
- Goulder *et al.* [1997a] is a review on CTL immune escape that discusses this epitope in the context of the difficulty in detection of immune escape – KRWIILGLNK and an R2K change, KKWIILGLNK, show little difference in titration curves, yet the K2 variants fail to bind to targets for more than 1 hour, while the R2 form can sensitize lysis by CTL for over 24 hours – minigene transfection experiments confirmed the importance of this for the CTL response.

HXB2 Location p24 (131–140)
Author Location p24 (260–269 HIV-2)
Epitope RRWIQLGLQK
Immunogen
Species (MHC) human (B27)
References Brander & Walker 1996

- HIV-2, HLA-B*2703, S. Rowland-Jones, pers. comm.

HXB2 Location p24 (131–140)
Author Location p24 (263–272 LAI)
Epitope KRWIILGLNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords dendritic cells
References Fan *et al.* 1997

- The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied.

HXB2 Location p24 (131–140)
Author Location Gag (263–272)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords epitope processing, dendritic cells
References Zheng *et al.* 1999

- Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone.
- Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway.
- The CTL response to p24 was measured in individuals with a response to B27-KRWIILGLNK.

HXB2 Location p24 (131–140)
Author Location p24 (263–272 LAI)
Epitope KRWIILGLNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords dynamics, TCR usage
References Wilson *et al.* 1998a

- HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed *in vivo*.
- Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls.
- Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases.

HXB2 Location p24 (131–140)
Author Location p24
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords review
References Rowland-Jones *et al.* 1997

- Described in this review as the first identified HIV CTL epitope.

HXB2 Location p24 (131–140)
Author Location p24 (263–272 LAI)
Epitope KRWIILGLNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Buseyne *et al.* 1993b

- Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.

HXB2 Location p24 (131–140)
Author Location p24 (263–272 LAI)
Epitope KRWIILGLNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords review
References McMichael & Walker 1994

- Review of HIV CTL epitopes.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIIMGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Klenerman *et al.* 1994

- Naturally occurring variant KRWIILGLNK may act as antagonist.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIIMGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Klenerman *et al.* 1995

- Naturally occurring variant KRWIILGLNK may act as antagonist.

HXB2 Location p24 (131–140)
Author Location p24 (265–274)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords dynamics, TCR usage
References Moss *et al.* 1995

- In one individual, TCR usage changed over time indicating that new populations of CTL can be recruited.
- TCR usage showed a CTL clonal response to this epitope that persisted over 5 years.
- CTL clones specific for HIV epitopes may represent between 0.2 and 1% of the total CD8+ population of T cells.

HXB2 Location p24 (131–140)
Author Location p24 (265–276)
Epitope KRWIILGLNK
Immunogen
Species (MHC) human (B27)
References Carreno *et al.* 1992

- Included in HLA-B27 binding peptide competition study.

HXB2 Location p24 (131–140)
Author Location p24 (265–274 SF2)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)

Keywords dynamics, review, immunodominance, escape
References Goulder *et al.* 1997a; Phillips *et al.* 1991

- Longitudinal study of CTL escape mutants – little variation was observed in the immunodominant B27 epitope, relative to B8 epitope.
- Goulder *et al.* [1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords review, escape
References Goulder *et al.* 1997a; Nietfeld *et al.* 1995

- Single point mutations were introduced and viral viability and CTL recognition tested – an Arg to Lys change at anchor position P2 abrogates binding to B27, but doesn't change viral viability *in vitro*.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIIMGNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords escape
References Nowak *et al.* 1995

- Longitudinal study of CTL response and immune escape – the form KRWIILGNK was also found, and both forms stimulate CTL.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIILGNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords inter-clade comparisons
References Durali *et al.* 1998

- Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia.
- Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested.
- Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag.
- Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef.
- Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env.
- One of the patients was shown to react to this epitope: KRWIILGNK.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIIMGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords review, immunodominance, escape
References Goulder *et al.* 1997f; Goulder *et al.* 1997a

- Six HLA-B27 donors studied make a strong response to this epitope.
- In 4/6 cases, this was the immunodominant or only CTL response.
- Two of the cases had an epitope switch to the form KKWIIMGLNK during a period of rapid decline to AIDS, following their asymptomatic period.
- The arginine to lysine switch is in an anchor residue, and results in immune escape due to severely diminished binding to the B27 molecule.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study in the context of CTL escape to fixation.

HXB2 Location p24 (131–140)
Author Location p24
Epitope KRWIILGLNK
Immunogen
Species (MHC) human (B27)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective.
- HIV-2 sequence: RRWIQLGLQK – this epitope was not HIV-1 and HIV-2 cross-reactive.

HXB2 Location p24 (131–140)
Author Location Gag (263–)
Epitope KRWIILGLNK
Immunogen computer prediction
Species (MHC) (B27)
Keywords inter-clade comparisons
References Schafer *et al.* 1998

- This study uses EpiMatrix for T cell epitope prediction to identify possible HLA-B27 and A-2 CTL epitopes in HIV.
- Based on EpiMatrix predictions, 28 peptides were synthesized and tested using T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule.
- Two of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV.
- This peptide sequence is not conserved between clades, but is found in most B clade isolates.

HXB2 Location p24 (131–140)
Author Location p24 (263–282)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Bernard *et al.* 1998

- This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population.
- No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs.
- Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XRXXXXXXXK is a B*2705 binding motif.

HXB2 Location p24 (131–140)
Author Location p24 (265–274 SF2)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B27+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/1 group 3.

HXB2 Location p24 (131–140)
Author Location p24 (263–272)
Epitope KRWIILGLNK
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B27)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Subject ML 1760 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, and gained responses to epitopes A2 SL(F/Y)NTVATL and B27 KRWII(L/M)GLNK post-seroconversion.

HXB2 Location p24 (131–140)
Author Location p24 (131–140)
Epitope KRWIILGLNK
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Day *et al.* 2001

HXB2 Location p24 (131–140)
Author Location p24 (260–299)
Epitope RRWIQLGLQK
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Day *et al.* 2001

HXB2 Location p24 (131–140)
Author Location p24 (131–140)
Epitope KRWIILGLNK
Epitope name KK10
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords responses in children, mother-to-infant transmission, immunodominance, escape, acute infection
References Goulder *et al.* 2001b

- 85% of B27+ adults have CTL that recognize this epitope, but only 2/6 children did.
- Responses to this dominant B27-restricted Gag epitope are present during the time of decreasing viral load in acute infection.
- Three children who shared B27 with their mothers did not respond to this epitope and inherited escape mutations from their mothers.
- A transmitted R132T anchor residue mutation abrogated binding to B27.
- In the three children infected with the non-binding KK10 variants, the dominant CTL specificity was still HLA-B27-restricted, but it was directed against an epitope in p17, IRLRPGGKK, only rarely recognized in adults when KRWIILGLNK is the dominant response.
- Mutations in this epitope were observed in autologous clones of subjects who were B27-positive with a higher frequency than those who were B27-negative (P = 0.0005)
- These mutations are being sexually transmitted in adult infections.

HXB2 Location p24 (131–140)
Author Location
Epitope KRWIILGLNK
Epitope name Gag-KK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B27, 2/3 (66%) recognized this epitope.

HXB2 Location p24 (131–140)
Author Location p24 (263–272 LAI)
Epitope KRWIIMGLNK
Subtype B

Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords HAART, ART, epitope processing, immunodominance
References Kelleher *et al.* 2001a

- Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in an intracellular context.
- RTV did not reduce antigen presentation and concentration of the two immunodominant Gag CTL epitopes (KRWIIMGLNK (B27) and SLYNTVATL (A2)).
- RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.

HXB2 Location p24 (131–140)
Author Location p24
Epitope KRWIILGLNK
Epitope name B27-KK10(p24)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
Donor MHC A24, A?, B7, B27; A30, A32, B18, B27
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef). Patient D also displayed the greatest response to B27-KK10(p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).

HXB2 Location p24 (131–140)
Author Location Gag (263–272)
Epitope KRWIILGLNK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (B27)
Donor MHC B27
Keywords inter-clade comparisons
References Currier *et al.* 2002a

- Cross-reactive responses were found in PBMC isolated from individuals infected with either B or CRF01_AE clade viruses, as determined by Elispot assays of target cells expressing recombinant vaccinia viruses expressing HIV-1 gag, env, nef and pol from many clades.
- Subject AIHP-6 (Thai, CDF01-AE infected) recognized this epitope. This subject showed cross-subtype CTL responses to gag constructs derived from subtypes A, B, C, D, F, G, and H, and this epitope was perfectly preserved in all of these but subtype A which had the sequence KRWMILGLNK.
- This subject didn't respond to a Gag CRF01 sequence which had a R->K mutation in position 2.

HXB2 Location p24 (131–140)
Author Location Gag
Epitope KRWIILGLNK
Epitope name KK10
Immunogen HIV-1 infection
Species (MHC) human (B27)
Donor MHC A26, B27
Assay type CD8 T-cell Elispot - IFNγ
Keywords responses in children, rate of progression, immunodominance, escape
References Feeney *et al.* 2004

- Viral load in a perinatally infected child remained low until emergence of an escape variant (kTwiilglnk) in the immunodominant CTL epitope KRWIILGLNK when the child was 7.4 years old. The emergence of this escape mutation was followed by an increase in viremia and an increase in the number of targeted CTL epitopes, measured again when the child was 9.2 years old. The timing suggests that the loss of recognition of this epitope may have resulted in the subsequent loss of immune control.
- The mutation krwillMglnk has been suggested to be compensatory and required for the emergence of the previously described escape mutation kKwillMglnk (Kelleher 2001). The L136M mutation does appear in this child, but not in conjunction with the R132T escape mutation.

HXB2 Location p24 (131–140)
Author Location
Epitope KRWIIMGLNK
Epitope name KK10
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords review, responses in children, vaccine-specific epitope characteristics, rate of progression, escape
References Goulder & Watkins 2004

- This paper is a review of the role of CTL in HIV infection, and it uses KK10 as an example of an epitope that has late escape mutations associated with loss of immune control of the virus and decline to AIDS.
- A study where a vaccine response to KK10 was stimulated in a individual who subsequently got infected and had rapid escape from the KK10 response and an unexpectedly high steady state viral load for a B27+ person is recounted as a cautionary note regarding the delicate balance of effects that might contribute to CTL mediated immune control.

HXB2 Location p24 (131–142)
Author Location p24 (265–276)
Epitope KRWIILGLNKIV
Immunogen Peptide-HLA interaction
Species (MHC) human (B27)
References Jardetzky *et al.* 1991

- Epitope examined in the context of peptide binding to HLA-B27.

HXB2 Location p24 (131–142)
Author Location p24 (263–274 LAI)
Epitope KRWIILGLNKIV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords dendritic cells
References Fan *et al.* 1997

- The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied.

HXB2 Location p24 (131–142)
Author Location p24 (131–142)
Epitope KRWIILGLNKIV
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (131–145)
Author Location p24 (SF2)
Epitope KRWILGLNKIVRMY
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ African American living in Boston with unknown HLA – this epitope did not fall within the three most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location p24 (131–145)
Author Location p24 (131–145 HXB2)
Epitope KRWIILGLNKIVRMY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (131–145)
Author Location p24 (263–277 LAI)
Epitope KRWIILGLNKIVMRY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A33)
References Buseyne *et al.* 1993b

- Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.

HXB2 Location p24 (131–145)
Author Location p24 (266–277)
Epitope KRWIILGLNKIVRMY
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* Gag
Species (MHC) human (B27)
References Nixon *et al.* 1988

- Gag CTL epitope mapped with rec gag-vaccinia and synthetic peptides.
- This was the first HIV-1 epitope to be mapped.

HXB2 Location p24 (131–145)
Author Location p24 (266–277 LAI)
Epitope KRWIILGLNKIVMRY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Meyerhans *et al.* 1991

- Longitudinal study showing persistence of epitope despite CTL activity.

HXB2 Location p24 (131–145)
Author Location p24 (265–279)
Epitope KRWIILGLNKIVRMY
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Nixon *et al.* 1990; Rowland-Jones *et al.* 1999

- HIV-1 and HIV-2 cross-reactive CTL clone, highly conserved epitope.
- Reviewed in Rowland-Jones99, notes that it did not appear cross-reactive with HIV-2 in Rowland-Jones98, HIV-2 form: RRWIQLGLQK.

HXB2 Location p24 (131–146)
Author Location p24 (265–279)
Epitope KRWIILGLNKIVRMYC
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Bouillot *et al.* 1989

- HLA-B27 restricted epitope also binds to HLA-A2 and HLA-B37 in solid phase assay.

HXB2 Location p24 (131–150)
Author Location p24 (263–282 SF2)
Epitope KRWIILGLNKIVRMYSPTSI
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 A-2 had CTL response to this peptide.
- The responding subject was HLA-A3, A32, B51, B62.

HXB2 Location p24 (131–150)
Author Location p24 (265–284 SF2)
Epitope KRWIILGLNKIVRMYSPTSI
Immunogen HIV-1 infection
Species (MHC) human (Bw62?)
References van Baalen *et al.* 1993

- Gag CTL epitope precursor frequencies estimated.

HXB2 Location p24 (131–152)
Author Location p24 (263–284 BH10)
Epitope KRWIILGLNKIVRMYSPTSILD
Immunogen HIV-1 infection
Species (MHC) human (Bw62)
References Johnson *et al.* 1991

- Gag CTL response studied in three individuals.

HXB2 Location p24 (132–140)
Author Location Gag (261–280)
Epitope RWIILGLNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
Donor MHC A24, A33, B14, B27; A2, A32, B27, B62
Assay type Chromium-release assay
Keywords genital and mucosal immunity
References Musey *et al.* 2003

- CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments.
- CD8+ T cell clones that recognize this epitope were derived from both blood and cervix from a woman, and the blood and semen from a man.

HXB2 Location p24 (132–145)
Author Location Gag
Epitope KWILGLNKIVRMY
Immunogen HIV-1 infection
Species (MHC) human
References Weekes *et al.* 1999a

- Peptide 728: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations.

HXB2 Location p24 (132–145)
Author Location Gag
Epitope KWILGLNKIVRMY
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords TCR usage
References Weekes *et al.* 1999b

- Peptide 728: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed the CD28 depleted cell population.
- HIV CTL responses to 3 Env and 2 Gag peptides were studied.
- The clonal composition of the TCR Vβ responses were studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ22.1.

HXB2 Location p24 (134–143)
Author Location Gag (266–275)
Epitope IILGLNKIVR
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A3, A11)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay

Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location p24 (134–143)
Author Location p24 (subtype B)
Epitope IILGLNKIVR
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A33)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among A, B and D clade viruses.

HXB2 Location p24 (135–142)
Author Location Gag (267–274)
Epitope ILGLNKIV
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A2)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the most frequently recognized of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location p24 (135–143)
Author Location Gag (267–275)
Epitope ILGLNKIVR
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A3, A11)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location p24 (135–145)
Author Location Gag (267–277)
Epitope ILGLNKIVRMY
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B7 supertype)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the most frequently recognized of the 31 epitopes that the vaccinated volunteers responded to.
- A response to this peptide was induced in three patients after immunization with lipopeptides alone (no adjuvant) after the third and the fourth boost, and induced in two patients after immunization with lipopeptides and QS21 adjuvant after the third boost. Variant IyGLNKIVRMY was also recognized in two patients.

HXB2 Location p24 (136–145)
Author Location p24 (268–277 LAI)
Epitope LGLNKIVRMY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Bw62)
Keywords review
References McMichael & Walker 1994

- Predicted from larger peptide.
- Review of HIV CTL epitopes.
- Also P. Johnson, pers. comm.

HXB2 Location p24 (136–146)

Author Location p24 (271–281)
Epitope LGLNKIVRMYS
Immunogen HIV-1 infection
Species (MHC) human (B62)
Keywords TCR usage
References Lubaki *et al.* 1997

- Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response.
- A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA molecules, indicating a polyclonal response.
- A subject who was B62+ had CTL that recognized this peptide, p17 KIRLRPGGKKKYKL, and one additional unknown epitope.
- The two clones that recognized this epitope used two different Vβ genes, further demonstrating a polyclonal response.

HXB2 Location p24 (136–146)
Author Location p24 (136–146)
Epitope LGLNKIVRMYS
Immunogen HIV-1 infection
Species (MHC) human (B62)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (136–150)
Author Location p24 (136–150 HXB2)
Epitope LGLNKIVRMYSPTSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized—the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (137–145)
Author Location p24 (C consensus)
Epitope GLNKIVRMY
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A2/-, B5802/62, Cw4/6
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ South African living in Durban, HLA A2/- B5802/62 Cw4/6 – this epitope did not fall within the three most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location p24 (137–145)
Author Location p24 (272–280 LAI)
Epitope GLNKIVRMY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1501)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*1501 epitope.

HXB2 Location p24 (137–145)
Author Location Gag (269–277 SUMA)
Epitope GLNKIVRMY
Epitope name Gag GY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1501)
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.

- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location p24 (137–145)
Author Location Gag (B con)
Epitope GLNKIVRMY
Epitope name GY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B15)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords variant cross-recognition or cross-neutralization
References Draenert *et al.* 2004c

- CD8 T-cell responses that persisted in individuals with advanced disease were studied; most of the optimal epitopes defined were recognized with intermediate to high avidity. On average 13 (range, 2-39) epitopic regons were targeted in an average of 6 proteins (range, 1-8). HAART resulted in decrease in antigen and reduction in gamma IFN EliSpot responses, suggesting active responses to autologous virus. Limited or no mutations within most viral epitopes suggest that persistent CTL through late disease do not exert strong immune selection pressure, yet the Elispot assays show robust responses, suggesting to the authors that gamma IFN based screening methods may not reveal functional CD8+ T-cell impairment in patients with AIDS.
- One subject recognized this epitope, with intermediate functional avidity. The autologous sequence matched the B consensus.

HXB2 Location p24 (137–145)
Author Location p24 (272–280 LAI)
Epitope GLNKIVRMY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B62)
Keywords review, escape
References Goulder *et al.* 1997a

- This paper is a review of CTL and immune evasion, but it presents a study of a shift from an HLA-A*0201 response to SLYNTVATL, to a B62 response to GLNKIVRMY.
- As long as a strong CTL response to SLYNTVATL was evident, the epitope variants SLFNTVATL or SLYNTIATL dominated the viral population – eventually the CTL response to the index peptide became undetectable, the CTL response shifted to a focus on GLNKIVRMY, and the index peptide SLYNTVATL once again established itself as the dominant form.

HXB2 Location p24 (137–145)
Author Location p24 (SF2)
Epitope GLNKIVRMY
Immunogen HIV-1 infection
Species (MHC) human (B62)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ African American living in Boston – this epitope did not fall within the three most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location p24 (137–145)
Author Location p24 (267–277 SF2)
Epitope GLNKIVRMY
Immunogen HIV-1 infection
Species (MHC) human (B62)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B62+ individuals that had a CTL response to this epitope broken down by group: 0/1 group 1, 0/1 group 2, and 1/1 group 3.

HXB2 Location p24 (137–145)
Author Location p24 (137–145)
Epitope GLNKIVRMY
Immunogen HIV-1 infection
Species (MHC) human (B62)
Keywords immunodominance
References Day *et al.* 2001

- No immunodominant responses were detected to four B62-restricted epitopes tested.

HXB2 Location p24 (137–145)
Author Location p24 (137–145)
Epitope GLNKIVRMY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B62)

Donor MHC A1, A3, B8, B62, Cw3, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location p24 (137–145)
Author Location Gag (269–277)
Epitope GLNKIVRMY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B62)
Donor MHC A2, A24, B27, B62
Assay type Chromium-release assay
Keywords TCR usage, genital and mucosal immunity
References Musey *et al.* 2003

- CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments.
- CD8+ T cell clones directed at this epitope were derived from blood, rectum and semen.
- The TCRbeta VDJ rearrangement of the CTL clones was Vβ22S1DJ1.2, demonstrating expansion of CTL clones in all three compartments from the same progenitor cell.

HXB2 Location p24 (143–150)
Author Location p24 (273–283 IIIB)
Epitope RMYSPTSI
Immunogen HIV-1 infection
Species (MHC) human (B*5201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5201 epitope.

HXB2 Location p24 (143–150)
Author Location p24 (273–283 IIIB)
Epitope RMYSPTSI
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (B52)
Keywords epitope processing, immunodominance, escape
References Brander *et al.* 1999

- Multiple natural variations in the SL9 flanking regions of the immunodominant epitope SLYNTVATL were tested and found not to adversely affect CTL recognition or prevent epitope processing, suggesting that viral escape from the HLA-A*0201-restricted CTL response against SLYNTVATL is probably not linked to variations in the flanking regions of this epitope.
- The CTL response to RMYSPTSI was used as a control.

HXB2 Location p24 (143–150)
Author Location p24 (273–283 IIIB)
Epitope RMYSPTSI
Immunogen HIV-1 infection
Species (MHC) human (B52)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope.

HXB2 Location p24 (143–150)
Author Location p24 (143–150)
Epitope RMYSPTSI
Immunogen HIV-1 infection
Species (MHC) human (B52)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (143–151)
Author Location Gag (275–283)
Epitope RMYSPTSIL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A2)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location p24 (144–151)
Author Location Gag (276–283)
Epitope MYSPTSIL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A24)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the most frequently recognized of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location p24 (151–170)
Author Location p24 (283–302 SF2)
Epitope LDIRQGPKEPFRDYVDRFYK
Immunogen HIV-1 infection
Species (MHC) human
References McAdam *et al.* 1998

HXB2 Location p24 (155–177)
Author Location p24 (287–309)
Epitope QGPKEPFRDYVDRFYKTLRAEQA
Immunogen Vaccine
Vector/Type: peptide *HIV component:* p24 Gag
Species (MHC) mouse
References Nakamura *et al.* 1997

- Mice immunized with this synthetic peptide generated specific CTLs, a proliferative response, and antibodies.
- The amino acids shown in the epitope field were based on the numbering provided by Nakamura *et al.*, and may not be correct.
- The CTL epitope was shown to be located in positions 291-300.

HXB2 Location p24 (157–178)
Author Location p24 (290–309)
Epitope PKEPFRDYVDRFYKTLRAEQAS
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Musey *et al.* 1997

- Cervical and peripheral blood derived CTL clones from an HIV-infected woman recognized this epitope.

HXB2 Location p24 (159–168)
Author Location Gag (291–300)
Epitope EPFRDYVDRF
Immunogen Vaccine
Vector/Type: DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18
Species (MHC) mouse (H-2^d)
Keywords Th1
References Billaut-Mulot *et al.* 2001

- DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization.
- Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost.
- Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-gamma)
- Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.

HXB2 Location p24 (159–168)
Author Location p24
Epitope EPFRDYVDRF
Epitope name E10F
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Gag
Species (MHC) mouse (H-2^d)
Assay type Chromium-release assay
References Bojak *et al.* 2002b

- Codon-optimized gag gene DNA vaccines were compared to wild type by vaccination of BALB/c mice. Codon optimized DNA gave a Th1 polarized Th response, a strong antibody response that persisted from more than 20 weeks, and CTL responses, while wild-type DNA induced weak and inconsistent immune respones.

HXB2 Location p24 (159–168)
Author Location
Epitope EPFRDYVDRF
Epitope name E10F
Immunogen Vaccine
Vector/Type: DNA, virus-like particle (VLP), polyepitope *HIV component:* Gag, p24 Gag, V3
Species (MHC) mouse (H-2L<sup>d<sup>)
Assay type cytokine production, Chromium-release assay
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance
References Wild *et al.* 2004

- A codon optimized gag DNA vaccine was compared to a myristylation defective gag and p24 alone, both of which lack signals for secretion from transfected cells. Gag-derived immunogens that were secreted as VLPs and those that remained intracellular (p24) each produced strong CTL responses, and

neither the size of antigen nor cellular trafficking and localization significantly influenced the strength of humoral and cellular immune activation. The formation and release of VLPs was not essential for eliciting strong CTL. BALB/c mice were given the DNA vaccine by i.m. administration of plasmid DNA for the prime and boost.
- Minigenes were made incorporating just one epitope, minitopes, carrying one of three murine class I eptiopes linked to the Ad2-E3 protein-derived signal peptide to allow access of the epitope to the ER. Weak induction of cellular immune resposes was observed, in contrast to the complex polyprotein. The E10F minigene did not produce a detectable CTL response.

HXB2 Location p24 (159–178)
Author Location Gag (291–310)
Epitope EPFRDYVDRFFKTLRAEQAT
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002
- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location p24 (159–178)
Author Location Gag (96ZM651.8)
Epitope EPFRDYVDRFFKTLRAEQAT
Immunogen
Species (MHC) human (B*44031)
Keywords inter-clade comparisons, immunodominance
References Novitsky *et al.* 2001
- This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort.
- 16 of 46 (34.8%) had CTL responses to one or more peptides within the second immunodominant region region of Gag (peptides SILDIKQGPKEPFRDYVDRF, EPFRDYVDRFFKTLRAEQAT, and FKTLRAEQATQEVKNWMTDT) with ELISPOT results median and range 500 (100 to 1,250) SFC/10^6 PBMC
- 3 of 6 (50%) carriers of HLA-B*44031 showed CTL responses to the peptide EPFRDYVDRFFKTLRAEQAT.

HXB2 Location p24 (160–169)
Author Location p24
Epitope PFRDYVDRFF
Epitope name PF-10
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, epitope processing, immunodominance, cross-presentation by different HLA
References Masemola *et al.* 2004b
- Highly targeted regions in Gag for CD8+ T-cells were defined for individuals with C clade infections in South Africa. Nine specific epitopes within the most reactive regions were characterized. This is one of five novel epitopes that were found among subtype C HIV-1 from African patients that hadn't previously been identified in B clade infections. Some epitopes were shown to be promiscuous, presented by multiple class I restricting alleles. The HLA restricting element for this optimal epitope was not determined due to limited material.

HXB2 Location p24 (161–169)
Author Location (C consensus)
Epitope FRDYVDRFF
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (Cw*1801)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004
- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This epitope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (161–170)
Author Location
Epitope FRDYVDRFFK
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c
- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls, ML1732.

HXB2 Location p24 (161–170)
Author Location p24 (subtype B, D)
Epitope FRDYVDRFYK
Subtype B, D

Immunogen HIV-1 infection
Species (MHC) human (B*1801)
References Ogg *et al.* 1998a

- Noted in Brander 1999, this database, to be B*1801, FRDYVDRFY.

HXB2 Location p24 (161–170)
Author Location p24 (subtype B, D)
Epitope FRDYVDRFYK
Subtype B, D
Immunogen HIV-1 infection
Species (MHC) human (B*1801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*1801 epitope.

HXB2 Location p24 (161–170)
Author Location p24 (161–170)
Epitope FRDYVDRFYK
Immunogen HIV-1 infection
Species (MHC) human (B18)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (161–170)
Author Location p24 (293–302)
Epitope FRDYVDRFYK
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B18)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- Variants FRDYVDRF(Y/F)K are specific for the B,D/A,C clades.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B18 women, 3/4 HEPS and 1/9 HIV-1 infected women recognized this epitope, likelihood ratio 5.3, p value 0.04, and HEPS women tended to respond to FRDYVDRFY/FK, while infected women tended to respond to YPLTFGWCY/F.
- The dominant response to this HLA allele was to this epitope for all 3/4 HEPS cases and for the single HIV-1 infected women that responded to this epitope.
- Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLNM/TLN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24.
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.

HXB2 Location p24 (161–170)
Author Location p24
Epitope FRDYVDRFYK
Subtype B, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade
HIV component: p17 Gag, p24 Gag
Species (MHC) human, macaque (B18)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location p24 (161–174)
Author Location p24 (161–174 HXB2)
Epitope FRDYVDRFYKTLRA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.

- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (161–180)
Author Location p24 (293–312 SF2)
Epitope FRDYVDRFYKTLRAEQASQD
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A2, A3, B8, B62.

HXB2 Location p24 (161–180)
Author Location p24 (293–312 SF2)
Epitope FRDYVDRFYKTLRAEQASQD
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location p24 (161–180)
Author Location p24 (293–312 SF2)
Epitope FRDYVDRFYKTLRAEQASQD
Immunogen HIV-1 infection
Species (MHC) human (B71)
References McAdam *et al.* 1998

HXB2 Location p24 (162–172)
Author Location p24 (296–306 subtype A)
Epitope RDYVDRFFKTL
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
Keywords inter-clade comparisons
References Dorrell *et al.* 1999

- CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa.
- This epitope is similar to the A24 DYVDRYFKT epitope found for B subtype, but CTL from this A subtype infection required the additional Arg – the B clade sequence change from F to Y diminished CTL reactivity.
- C. Brander notes that this is an A*2402 epitope in the 1999 database.

HXB2 Location p24 (162–172)
Author Location p24 (296–306 subtype A)
Epitope RDYVDRFFKTL
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*2402 epitope.

HXB2 Location p24 (162–172)
Author Location p24 (296–306)
Epitope RDYVDRFFKTL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A24)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-A24 women, 0/4 HEPS and 6/10 HIV-1 infected women recognized this epitope, likelihood ratio 7.2, p value 0.03, and (R)YL(R/K)DQQLL tended to be reactive in HEPS and infected women, RDYVDRFFKTL in infected women only.
- The dominant response to this HLA allele was to this epitope in all of the 6/10 HIV-1 infected women.
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.
- Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion.

HXB2 Location p24 (162–172)
Author Location p24 (293–312 LAI)
Epitope RDYVDRFYKTL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4402)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4402 epitope.

HXB2 Location p24 (162–172)

Author Location p24 (162–172)
Epitope RDYVDRFYKTL
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (162–172)
Author Location p24 (162–172)
Epitope RDYVDRFYKTL
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Day *et al.* 2001

HXB2 Location p24 (162–172)
Author Location p24
Epitope RDYVDRFYKTL
Subtype B, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human, macaque (B44)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location p24 (162–172)
Author Location Gag (B con)
Epitope RDYVDRFYKTL
Epitope name RL11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords variant cross-recognition or cross-neutralization
References Draenert *et al.* 2004c

- CD8 T-cell responses that persisted in individuals with advanced disease were studied; most of the optimal epitopes defined were recognized with intermediate to high avidity. On average 13 (range, 2-39) epitopic regons were targeted in an average of 6 proteins (range, 1-8). HAART resulted in decrease in antigen and reduction in gamma IFN EliSpot responses, suggesting active responses to autologous virus. Limited or no mutations within most viral epitopes suggest that persistent CTL through late disease do not exert strong immune selection pressure, yet the Elispot assays show robust responses, suggesting to the authors that gamma IFN based screening methods may not reveal functional CD8+ T-cell impairment in patients with AIDS.
- One subject recognized this epitope, with low functional avidity. The autologous sequence matched the B consensus.

HXB2 Location p24 (162–172)
Author Location p24 (293–312 LAI)
Epitope RDYVDRFYKTL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44, A26, B70)
References Ogg *et al.* 1998a

HXB2 Location p24 (163–171)
Author Location Gag (295–303 SUMA)
Epitope DYVDRFYKT
Epitope name Gag DT9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location p24 (163–172)
Author Location p24 (163–172)
Epitope DYVDRFYKTL
Immunogen HIV-1 infection
Species (MHC) human (A24)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (163–173)
Author Location Gag (297–307 SF2)
Epitope DYVDRFYKTLR
Subtype B
Immunogen HIV-1 infection, computer prediction
Species (MHC) human (A*3303)
Assay type Chromium-release assay
Keywords binding affinity, computational epitope prediction
References Hossain *et al.* 2003

- HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing.
- This epitope is one of the 2/6 peptides that could induce CTL responses in the PBMC of infected individuals, but was not properly processed in a vaccinia-HIV infected target cell.

HXB2 Location p24 (164–172)
Author Location Gag (296–304)
Epitope YVDRFYKTL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0207)
Donor MHC A*0207
Keywords inter-clade comparisons
References Currier *et al.* 2002a

- Cross-reactive responses were found in PBMC isolated from individuals infected with either B or CRF01_AE clade viruses, as determined by Elispot assays of target cells expressing recombinant vaccinia viruses expressing HIV-1 gag, env, nef and pol from many clades.
- The Thai subject VAIP-4 demonstrated broad CTL cross-reactivity towards gag constructs derived from subtypes A, B, C, D, F, G, H, and CRF-01_AE. Sequence alignments of this epitope showed conservation for clades B and D, and Y->F substitutions at position 6 for subtypes A, C, CDR01-AE, F, G, and H. YVDRFYKTL and the variant epitope YVDRFFKTL are recognized equally well.

HXB2 Location p24 (164–172)
Author Location p24 (164–172)
Epitope YVDRFYKTL
Immunogen HIV-1 infection
Species (MHC) human (A*0207)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p24 (164–172)
Author Location p24 (298–306 subtype A)
Epitope YVDRFFKTL
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (A26, B70)
Keywords inter-clade comparisons
References Dorrell *et al.* 1999

- CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa.
- This CTL epitope is conserved in A and C subtype, and B clade sequences tend to have a change from F to Y, YVDRFYKTL – both variants showed strong CTL reactivity.
- CTL reacted with targets presenting either in the context A26 or B70 – the epitope has the HLA-26 motif of Val at position 2 and Leu at the carboxy terminus, and the B70 anchor residue motif is unknown.

HXB2 Location p24 (164–172)
Author Location Gag (298–306 subtype A)
Epitope YVDRFFKTL
Subtype A
Immunogen HIV-1 infection, in vitro stimulation or selection
Species (MHC) human (A26, B70)
Keywords inter-clade comparisons
References Dorrell *et al.* 2001

- In vitro restimulation of CTL specific for dominant epitopes from infected individuals is possible using recombinant modified vaccinia virus Ankara (MVA) carrying A or D subtype HIV-1 Gag proteins.

HXB2 Location p24 (164–172)
Author Location p24
Epitope YVDRFFKTL
Epitope name YL-9
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, epitope processing, immunodominance, cross-presentation by different HLA
References Masemola *et al.* 2004b

- Highly targeted regions in Gag for CD8+ T-cells were defined for individuals with C clade infections in South Africa. Nine specific epitopes within the most reactive regions were characterized.
- YVDRFFKTL was presented by B*15, which is more common in Zulus than Caucasians (0.153 versus 0.079). This epitope had previously identified in B clade infections.

HXB2 Location p24 (164–172)
Author Location Gag (296–304 96ZM651.8)
Epitope YVDRFFKRL
Immunogen

Species (MHC) human (B*1510, B70)
Keywords inter-clade comparisons
References Novitsky *et al.* 2001

- This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort.
- 4 subjects who responsed to the CTL epitope YVDRFFKTL – all were HLA-B*1510 and also shared HLA-Cw03, suggesting linkage disequilibrium.
- An HIV-1 B variant of the epitope YVDRFYKTL has been described, and was recognized by CTL from an HIV-1 subtype A-infected patient, and the HLA restriction of the epitope was suggested to be A26 or B70 – HLA-B*1510 is equivalent to the serological specificity HLA B70.

HXB2 Location p24 (164–172)
Author Location p24 (164–172)
Epitope YVDRFYKTL
Immunogen HIV-1 infection
Species (MHC) human (B70)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (164–172)
Author Location p24 (164–172)
Epitope YVDRFFKTL
Immunogen
Species (MHC) human (Cw*0303)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p24 (164–172)
Author Location p24 (164–172)
Epitope YVDRFFKTL
Immunogen
Species (MHC) human (Cw*0304)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p24 (164–172)
Author Location (C consensus)
Epitope YVDRFFKTL
Epitope name YL9
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (Cw*0304)
Donor MHC A*3402, B*0801, B*4403, Cw*0304, Cw*0401
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This epitope was one of two used to illustrate how specific epitopes were characterized with regard to defining the optimal epitope and the HLA restricting element. HLA allelic associations in the population with peptide recognition was highly predictive of the epitope within the 15 mer.

HXB2 Location p24 (165–178)
Author Location p24 (165–177 HXB2)
Epitope VDRFYKTLRAEQAS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (166–174)
Author Location p24 (298–306 LAI)
Epitope DRFYKTLRA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1402)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*1402 epitope.

HXB2 Location p24 (166–174)
Author Location p24
Epitope DRFFKTLRA
Epitope name DA-9
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1403)
Country South Africa.

Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, epitope processing, immunodominance, cross-presentation by different HLA
References Masemola *et al.* 2004b

- Highly targeted regions in Gag for CD8+ T-cells were defined for individuals with C clade infections in South Africa. Nine specific epitopes within the most reactive regions were characterized.
- DRFFKTLRA was presented by B*14, which is more common in Zulus than Caucasians (0.066 versus 0.038). This epitope had previously identified in B clade infections.

HXB2 Location p24 (166–174)
Author Location p24 (298–306 IIIB)
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords responses in children, mother-to-infant transmission
References Wilson *et al.* 1996

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.
- DRFYKILRA, a naturally occurring variant, was found in mother, and is recognized although less reactive.
- DQFYKTLRA, a naturally occurring variant, was found in infant and is not recognized.

HXB2 Location p24 (166–174)
Author Location p24 (298–306 IIIB)
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Cao *et al.* 1997a

- The consensus peptide for clades B and D is DRFYKTLRA.
- The consensus peptide for clades A and C is DRFFKTLRA and it is equally reactive.

HXB2 Location p24 (166–174)
Author Location p24 (298–306 HXB2)
Epitope DRFYKTLRA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords kinetics
References Yang *et al.* 1997b

- A chimeric universal T cell receptor was created by linking CD4 or an HIV-specific anti-gp41 Ig sequence to the signaling domain of the T cell receptor chain ζ, and transducing into CD8+ cells.
- The response using universal-receptor-bearing CD8+ cells to lyse infected cells *in vitro* was comparable to the natural occurring responses of CTL-clones from HIV+ individuals in terms of kinetics and efficiency.
- A CTL clone specific for this epitope was used for the comparison.

HXB2 Location p24 (166–174)
Author Location p24
Epitope DRFWKTLRA
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B14)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The D subtype consensus is identical to the B clade epitope.
- The A subtype consensus is drFfKtLRA.

HXB2 Location p24 (166–174)
Author Location p24 (298–306 LAI)
Epitope DRFYKTLRA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Harrer *et al.* 1996b

HXB2 Location p24 (166–174)
Author Location p24 (298–306)
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Yang *et al.* 1996

- CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL.
- Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones.
- The distinction was thought to be due to lower expression of RT relative to Env and Gag.
- CTL can lyse infected cells early after infection, possibly prior to viral production.

HXB2 Location p24 (166–174)
Author Location p24 (298–306)
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
Assay type CTL suppression of replication
References Yang *et al.* 1997a

- CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*.
- CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation.
- CTL suppress HIV replication more efficiently in HLA-matched cells.

HXB2 Location p24 (166–174)
Author Location p24 (298–306)
Epitope DRFYKTLRA
Immunogen in vitro stimulation or selection
Species (MHC) human (B14)
Keywords dendritic cells
References Zarling *et al.* 1999

- This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses.
- Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA.
- A weak response to KLTPLCVSL was stimulated using macrophages as the APC.
- No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.

HXB2 Location p24 (166–174)
Author Location p24
Epitope DRFYKLTRA
Immunogen
Species (MHC) human (B14)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective.
- HIV-2 sequence: DRFYKSLRA is cross-reactive, Harrer *et al.* [1993]

HXB2 Location p24 (166–174)
Author Location p24 (298–306 IIIB)
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- DRFYKILRA and DQFYKTLRA were escape mutants.

HXB2 Location p24 (166–174)
Author Location p24 (SF2)
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in 2/5 HIV+ individuals who were HLA B14 living in Boston – this epitope did not fall within the three most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location p24 (166–174)
Author Location p24 (SF2)
Epitope DRFYKTLRA
Epitope name DA9
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords acute infection
References Goulder *et al.* 2001a

- Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia.
- A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation.

HXB2 Location p24 (166–174)
Author Location p24 (166–174)
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (166–174)
Author Location p24 (298–306 SF2)
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B14+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/2 group 2, and 0/0 group 3.

HXB2 Location p24 (166–174)
Author Location p24 (298–306)
Epitope DRFFKTLRA
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B14)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- Variants DRF(F/W)KTLRA are specific for clades A/B.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B14 women, 0/4 HEPS and 6/7 HIV-1 infected women recognized this epitope, likelihood ratio 14.4, p value 0.004 and HEPS women tended to respond to DLNMML-NIV/DLNTMLNVV, while infected women tended to respond to DRF(F/W)KTLRA.
- The dominant response to this HLA allele was to this epitope for all of the 6/7 HIV-1 infected women.
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.

HXB2 Location p24 (166–174)
Author Location p24 (SF2)
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.

HXB2 Location p24 (166–174)
Author Location p24
Epitope DRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords epitope processing
References Cao *et al.* 2002

- AC13 is a B14 restricted CTL clone that recognizes DRFYK-TLRA.
- CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.

HXB2 Location p24 (166–174)
Author Location p24
Epitope DRFWKTLRA
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002

- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.
- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location p24 (166–174)
Author Location p24
Epitope DRFYKTLRA
Subtype B, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human (B14)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location p24 (166–174)
Author Location p24 (166–174)
Epitope DRFYKTLRA
Subtype B
Immunogen HIV-1 infection

Species (MHC) human (B14)
Donor MHC A1, A3, B7, B14, Cw*0702, Cw*0802; A1, A1, B8, B14, Cw7, Cw8
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- This epitope was recognized in two subjects early in infection, presented by B14 in each case.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location p24 (166–174)
Author Location p24 (166–174)
Epitope DRFYKTLRA
Epitope name Gag/p24-DA9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Assay type Chromium-release assay
Keywords binding affinity, TCR usage, characterizing CD8+ T cell responses
References Yang *et al.* 2003b

- Killing efficiency of CTLs and their ability to suppress viral replication is shown to depend more on epitope specificity than to antigenic avidity. Different clones recognizing the same epitope had similar killing efficiency despite their variation in avidity. Nef specific CTL clones tended to be most inhibitory, followed by Gag, then by RT specific clones, regardless of avidity.
- 1/14 CTL T-cell clones tested were specific for Gag/p24-DA9. Under conditions of excess peptide (100ug/ml), there was no difference in their lytic potential; all possessed similar effector capacity. Avidity was measured as the sensitizing dose of peptide required for 50% of maximal killing (SD50), which varied from 20 pg/ml to 100 ng/ml, over four orders of magnitude for all 14 epitopes. The SD50 value for Gag/p24-DA9 was 100,000 pg/ml, it had the lowest avidity of the 14 tested.

HXB2 Location p24 (166–174)
Author Location (C consensus)
Epitope DRFFKTLRA
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B14)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (166–174)
Author Location (B consensus)
Epitope DRFYKTLRA
Epitope name DA9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Donor MHC A28, A29, B14, B44, Cw8; A25, A32, B08, B14, Cw7, Cw8; A03, B14, B60, Cw3, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 3/9 individuals recognized this epitope, presented by HLA-B14.

HXB2 Location p24 (166–174)
Author Location p24 (subtype B)
Epitope DRFYKTLRA
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B14, B*1402)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.

- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among B and D clade viruses.
- The Clade A version of the epitope, DRFFKLTRA, was preferentially recognized by CTL.
- This epitope was recognized by two different exposed and uninfected prostitutes.

HXB2 Location p24 (166–175)
Author Location p24 (298–306 HX10)
Epitope DRFYKTLRAE
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords immunodominance
References Wagner *et al.* 1999

- The immunodominant CTL response in a long-term survivor was to this highly conserved and functionally relevant epitope.
- By testing mutations in an HXB2 background, it was found that all mutations within the epitope that abrogated CTL recognition also abolished viral infectivity.
- The epitope in this study overlaps the major homology region for which highly conserved residues exist in all known lenti- and onco-viruses and yeast transposons.
- Patient was part of the study in Harrer *et al.* [1996a]

HXB2 Location p24 (166–175)
Author Location Gag (298–307)
Epitope DRFYKTRAE
Immunogen HIV-1 infection
Species (MHC) human (B14)
Donor MHC A24, A33, B14, B27
Assay type Chromium-release assay
Keywords TCR usage, genital and mucosal immunity
References Musey *et al.* 2003

- CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments.
- CD8+ T cell clones directed at this epitope were derived from blood and cervix.

HXB2 Location p24 (166–176)
Author Location Gag (295–305 BORI)
Epitope DRFYKTLRAEQ
Epitope name Gag DQ11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1402)
Donor MHC A*2902, B*1402, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, acute infection, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient BORI had high viral loads and rapid CD4 decline. BORI mounted 8 detected responses. BORI did not control viral replication well, and escape mutations occurred early and in most epitopes, 6/7 that were precisely identified.
- DRFYKTLRAEQ didn't vary. There was no response in acute infection to this epitope, but the response was detectable by early infection.

HXB2 Location p24 (169–185)
Author Location p24 (169–184 HXB2)
Epitope YKTLRAEQASQDVKNWN
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- Responses to this peptide were detected in 17% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p24 (169–188)
Author Location Gag (301–320)
Epitope FKTLRAEQATQDVKNWMTDT
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location p24 (169–188)
Author Location Gag (301–320)
Epitope YKTLRAEQASQEVKNWMTET
Immunogen HIV-1 infection
Species (MHC) human (B57)
Donor MHC A1, A66, B52, B57
Assay type Chromium-release assay
Keywords TCR usage, genital and mucosal immunity
References Musey *et al.* 2003

- CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments.
- CD8+ T cell clones directed at this epitope were derived from blood and rectum.

HXB2 Location p24 (171–180)
Author Location p24
Epitope TLRAEQATQD
Epitope name TD-10
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (Cw*0304)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, epitope processing, immunodominance, cross-presentation by different HLA
References Masemola *et al.* 2004b

- Highly targeted regions in Gag for CD8+ T-cells were defined for individuals with C clade infections in South Africa. Nine specific epitopes within the most reactive regions were characterized. This is one of five novel epitopes that were found among subtype C HIV-1 from African patients that hadn't previously been identified in B clade infections. Some epitopes were shown to be promiscuous, presented by multiple class I restricting alleles.
- TLRAEQATQD was presented by Cw*03 and newly identified in this study; Cw*03 is more common in Zulus than Caucasians (0.157 versus 0.101).

HXB2 Location p24 (173–181)
Author Location
Epitope RAEQASQEV
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls ML1792.

HXB2 Location p24 (173–181)
Author Location Gag (305–313 SUMA)
Epitope RAEQASQEV
Epitope name Gag RV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw*0802)
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location p24 (173–181)
Author Location p24 (305–313)
Epitope RAEQASQEV
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
References Johnson *et al.* 1991

- Originally reported as HLA-B14 restricted, but subsequently found not to be presented by cells transfected with B14.
- Thought to be HLA-Cw8 restricted (C. Brander and B. Walker)

HXB2 Location p24 (173–181)
Author Location p24
Epitope RAEQASQEV
Immunogen HIV-1 exposed seronegative
Species (MHC) human (Cw8)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A subtype consensus is RAeQAtQEV.
- The D subtype consensus is RAEQsQdV.
- Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)

HXB2 Location p24 (173–181)
Author Location p24 (305–313)
Epitope RAEQASQEV
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
References Price *et al.* 1995

- Study of cytokines released by HIV-1 specific activated CTL.
- Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)

HXB2 Location p24 (173–181)
Author Location p24 (305–313)
Epitope RAEQASQEV
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
References Lubaki *et al.* 1997

- Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response.
- A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response.
- Despite this being a well defined conserved epitope, and thought to be presented by B14, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 PQDLNTMLN.
- Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)

HXB2 Location p24 (173–181)
Author Location p24 (305–313)
Epitope RAEQASQEV
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (Cw8)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location p24 (174–184)
Author Location p24 (306–316 LAI)
Epitope AEQASQDVKNW
Subtype B
Immunogen
Species (MHC) human (B*4402)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4402 epitope.

HXB2 Location p24 (174–184)
Author Location p24 (306–316 LAI)
Epitope AEQASQDVKNW
Subtype B
Immunogen
Species (MHC) human (B*4402, B44)
References Brander & Walker 1997

- Pers. comm. from D. Lewinsohn to C. Brander and B. Walker, C Brander *et al.*, this database, 1999.

HXB2 Location p24 (174–184)
Author Location Gag (306–316)
Epitope AEQASQEVKNW
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Brodie *et al.* 1999

- The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptively transferring them.
- The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects.

HXB2 Location p24 (174–184)
Author Location p24 (306–316)
Epitope AEQASQEVKNW
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Brodie *et al.* 2000

- Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL.
- Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication.
- The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism.
- This study provides a methodology for tracking and studying antigen specific CTL *in vivo*

HXB2 Location p24 (174–184)
Author Location p24 (306–316 LAI)
Epitope AEQASQDVKNW
Epitope name G3
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.

- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location p24 (174–184)
Author Location p24 (174–184)
Epitope AEQASQDVKNW
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Day *et al.* 2001

- B44-restricted CTL response was strongest to this epitope in one individual.

HXB2 Location p24 (174–184)
Author Location p24
Epitope AEQASQDVKNW
Epitope name B44-AW11(p24)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44)
Donor MHC A32, A?, B44, B?
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient B displayed the greatest response to epitope B44-AW11(p24) and also responded to A32-PW10(RT) in both PB and LN samples, while a third response against epitope A32-RW10(gp120) was only detected in the LN sample.

HXB2 Location p24 (174–184)
Author Location Gag (B con)
Epitope AEQASQEVKNW
Epitope name AW11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords variant cross-recognition or cross-neutralization
References Draenert *et al.* 2004c

- CD8 T-cell responses that persisted in individuals with advanced disease were studied; most of the optimal epitopes defined were recognized with intermediate to high avidity. On average 13 (range, 2-39) epitopic regons were targeted in an average of 6 proteins (range, 1-8). HAART resulted in decrease in antigen and reduction in gamma IFN EliSpot responses, suggesting active responses to autologous virus. Limited or no mutations within most viral epitopes suggest that persistent CTL through late disease do not exert strong immune selection pressure, yet the Elispot assays show robust responses, suggesting to the authors that gamma IFN based screening methods may not reveal functional CD8+ T-cell impairment in patients with AIDS.
- One subject recognized this epitope, with low functional avidity. The autologous sequence matched the B consensus.

HXB2 Location p24 (174–184)
Author Location (B consensus)
Epitope AEQASQDVKNW
Epitope name AW11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44)
Donor MHC A02, A11, B18, B44, Cw5, Cw12; A28, A29, B14, B44, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 2/9 individuals recognized this epitope, presented by HLA-B44.

HXB2 Location p24 (174–185)
Author Location p24 (174–185)
Epitope AEQASQEVKNWM
Immunogen
Species (MHC) human (Cw*05)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p24 (175–186)

Author Location p24 (307–318)
Epitope EQASQEVKNWMT
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Quayle *et al.* 1998

- HIV is found in semen both as cell-associated and cell-free forms, and HIV-specific CTL could be found in the semen of 5/5 men with CD4 greater than 500 – 3 of the men were analyzed in detail and had broad CTL to gag, env and pol.
- Two CTL lines from one donor recognized this epitope.
- Isolation of CTLs specific to HIV in both male and female urinal tracts provide evidence that virus-specific lymphocytes come from the urogenital mucosa, and the authors speculate that CTL in mucosal tissues may be correlated with lower viral load in semen and reduced transmission.

HXB2 Location p24 (176–184)
Author Location Gag
Epitope QASQEVKNW
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement, epitope processing, characterizing CD8+ T cell responses
References Beattie *et al.* 2004

- This study compared CD8+ T cell EliSpot reponses to 58 Gag peptides that were optimal epitopes, with responses to overlapping 15 mers that spanned Gag. When screening for HIV-1-specific CD8 T-cell responses from 49 HIV+ people, overlapping 15-mer peptide pools revealed several novel responses that would have been missed using predefined CD8 epitopes. However, the 15-mer pools often missed low-level responses to predefined epitopes, especially when the epitope was located centrally in the 15-mer peptide, and the overall level of response to the 15 mers was generally lower(mean 1.4 fivel fold dilutions lower, range 0-3).
- In one individual, a response to QASQEVKNW could be detected at a concentration of 0.2 ug/ml, while a response to RAEQASQEVKNWMTE required 25 ug/ml for detection.

HXB2 Location p24 (176–184)
Author Location p24 (308–316 LAI)
Epitope QASQEVKNW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5301)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5301 epitope.

HXB2 Location p24 (176–184)
Author Location
Epitope QASQEVKNW
Epitope name Gag-QW9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5301, B57)
Donor MHC 01RCH59 A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subject 01RCH59 was Hispanic, was not on HAART, viral load 5100, CD4 count 349, and she also recognized PIQKETWETW, RT(392-401), A*3201.
- Among HIV+ individuals who carried HLA B*5301, 11/15 (73%) recognized this epitope.
- Among HIV+ individuals who carried HLA B57, 3/6 (60%) recognized this epitope.

HXB2 Location p24 (176–184)
Author Location p24 (309–317 LAI)
Epitope QASQEVKNW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
References Goulder *et al.* 1996b

- Recognition of this peptide by two long-term non-progressors.
- Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations.
- Described as B*5701 in C. Brander *et al.*, this database, 1999.

HXB2 Location p24 (176–184)
Author Location p24 (311–319 LAI)
Epitope QASQEVKNW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5701 epitope.

HXB2 Location p24 (176–184)
Author Location
Epitope QASQEVKNW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords rate of progression, immunodominance
References Migueles & Connors 2001

- HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.
- Only QASQEVKNW was recognized in all of the LTNP's tested.

HXB2 Location p24 (176–184)
Author Location
Epitope QASQEVKNW

Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords rate of progression, immunodominance
References Migueles & Connors 2001

- CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their CD8+ T-cell response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, or QASQEVKNW.
- CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia.
- The HLA-A*0201 SLYNTVATL epitope response was not as strong individuals that carried both A2, B57.

HXB2 Location p24 (176–184)
Author Location Gag (308–316)
Epitope QASQEVKNW
Epitope name QW9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Assay type Intracellular cytokine staining, Flow cytometric CTL assay
Keywords rate of progression, escape
References Migueles *et al.* 2003

- cDNA Gag sequences from a set of 17 HLA-B*5701+ progressors and 10 LTNPs were obtained, and the variation in four p24 B*5701 epitopes examined. Sequence variants were more common ($p < 0.01$) in the epitopes in the progressors (median 3, range 1-7) than LTNPs (median 2, range 0-4).
- In general use of the autologous protein in a target cell did not diminish the overall CD8+ T-cell responses.
- The substituion E312D (qasqDvknw) was common in progressors (8/17) and rare in LTNP (1/8) ($p = 0.06$). qasqDvknw and qasqEvknw peptides were made; this mutation does not affect binding to B*57. 2/4 progressors that carried only the D variant could not recognize the D variant peptide, but could recognize the E variant peptide, demonstrating immune escape.

HXB2 Location p24 (176–184)
Author Location (C consensus)
Epitope QATQDVKNW
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*5801)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (176–184)
Author Location p24 (308–316 LAI)
Epitope QASQEVKNW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B53)
References Buseyne *et al.* 1997

- Minimal sequence determined through epitope mapping.
- This is a relatively conserved epitope.
- HLA-Cw*0401 was defined as the restricting element, but cells that carry Cw*0401 varied in their ability to present this epitope – this could be the result of diminished cell-surface expression of Cw*0401 in some cells.
- The HLA presenting molecule for this epitope was originally described as Cw*0401, but subsequent experiments with an HLA B53+ C4- cell line and with C1R cells transfected with HLA-B53 have shown that the HLA restricting element is HLA-B53 (F. Buseyne, pers. comm. 2000)

HXB2 Location p24 (176–184)
Author Location (LAI)
Epitope QASQEVKNW
Subtype B
Immunogen
Species (MHC) human (B53)
Keywords optimal epitope
References Buseyne 1999; Frahm *et al.* 2004

HXB2 Location p24 (176–184)
Author Location p24 (NL43)
Epitope QASQEVKNW
Epitope name QW9
Immunogen in vitro stimulation or selection
Species (MHC) human (B53)
Keywords epitope processing, dendritic cells
References Buseyne *et al.* 2001

- Exogenous presentation or cross-presentation of epitopes by antigen presenting cells (APC) without protein synthesis is an alternative pathway for CTL epitope processing that may be important in the initial generation of viral specific CTL.
- Dendritic cells treated with AZT to inhibit protein synthesis were able to elicit a strong specific CTL response in QASQEVKNW specific CTL clone 141 without protein synthesis, while macrophages demonstrated a decreased presentation efficiency.
- Exogenous Gag epitope presentation was Env-dependent and required receptor-dependent fusion.

HXB2 Location p24 (176–184)
Author Location p24 (308–316)
Epitope QATQEVKNW
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B53)

Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B53 women, 1/2 HEPS and 7/9 HIV-1 infected women recognized this epitope.

HXB2 Location p24 (176–184)
Author Location p24 (308–316 subtype A consensus)
Epitope QATQEVKNM
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (B53)
Keywords binding affinity, inter-clade comparisons
References Dorrell *et al.* 2001

- In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays.
- Two of the new epitopes lacked the predicted P2 anchors, DTINEEAAEW and QATQEVKNM, and bound to B53 with high affinity, thus extending the anchor residue motif for B53 and the related B35.
- While S, T, and P could all fit into the HLA-B35 or HLA-B53 B pocket and form a hydrogen bond, A would not form a bond, so the authors propose compensatory interactions account for the high affinity of QATQEVKNM for B53.
- QATQEVKNM was recognized in 6/7 HLA-B53 subjects.
- Cross-recognition of QATQEVKNM was not studied here, but it was noted that both the A, QATQEVKNM, and B, QASQDVKNW, subtype version of this epitope, are also presented by HLA-B57 and B58, common HLA alleles in Africans.

HXB2 Location p24 (176–184)
Author Location Gag (304–321 B con)
Epitope QASQEVKNW
Epitope name QW9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B53, B58)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords variant cross-recognition or cross-neutralization
References Draenert *et al.* 2004c

- CD8 T-cell responses that persisted in individuals with advanced disease were studied; most of the optimal epitopes defined were recognized with intermediate to high avidity. On average 13 (range, 2-39) epitopic regons were targeted in an average of 6 proteins (range, 1-8). HAART resulted in decrease in antigen and reduction in gamma IFN EliSpot responses, suggesting active responses to autologous virus. Limited or no mutations within most viral epitopes suggest that persistent CTL through late disease do not exert strong immune selection pressure, yet the Elispot assays show robust responses, suggesting to the authors that gamma IFN based screening methods may not reveal functional CD8+ T-cell impairment in patients with AIDS.
- Two subjects recognized this epitope, with high functional avidity. Autologous sequence revelaed no substitutions in this epitope compared to the B consensus.

HXB2 Location p24 (176–184)
Author Location Gag (SF2)
Epitope QASQEVKNW
Epitope name QW9
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords acute infection
References Goulder *et al.* 2001a

- This peptide elicited a weak CTL response during acute infection of patient PI004.
- Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.

HXB2 Location p24 (176–184)
Author Location p24 (176–184)
Epitope QASQEVKNW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 6/7 patients recognized this epitope.

HXB2 Location p24 (176–184)
Author Location (LAI)
Epitope QASQEVKNW
Subtype B
Immunogen
Species (MHC) human (Cw4)
References Buseyne 1999

HXB2 Location p24 (176–184)
Author Location p24 (176–184)
Epitope QASGEVKNW
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (Cw4)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location p24 (176–185)
Author Location p24 (311–319 SF2)
Epitope QASKEVKNWV
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/2 group 3.

HXB2 Location p24 (177–185)
Author Location p24 (177–185)
Epitope ATQEVKNWM
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B53)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- Variants A(T/S)QEVKNWM are specific for the A/B clades.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B53 women, 1/2 HEPS and 5/9 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in the 1/2 HEPS case and in only one of the 5/9 HIV-1 infected women.

HXB2 Location p24 (180–189)
Author Location p24 (313–322)
Epitope EVKNWMTETL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B53)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location p24 (181–190)
Author Location p24 (313–322 LAI)
Epitope VKNWMTETLL
Subtype B
Immunogen
Species (MHC) human (B8)
References Brander & Walker 1996

- P. Johnson, pers. comm.

HXB2 Location p24 (191–205)
Author Location Gag (320–328 BH10, LAI)
Epitope VQNANPDCKTILKAL
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is TLLVQNANP) has similarity with growth differentiation factor 11, fragment THLVQQANP.

HXB2 Location p24 (191–205)
Author Location p24 (191–205)
Epitope VQNANPDCKTILKAL
Immunogen HIV-1 infection
Species (MHC) human (B51)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (191–205)
Author Location p24 (323–337)
Epitope VQNANPDCKTILKAL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Nixon & McMichael 1991

- Two CTL epitopes defined (see also p17(21-35))

HXB2 Location p24 (191–205)
Author Location p24 (325–339 SF2)

Epitope VQNANPDCKTILKAL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords review, immunodominance, escape
References Goulder *et al.* 1997a; Phillips *et al.* 1991

- Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to the B8 epitopes, which varied over time.
- Goulder *et al.* [1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients.

HXB2 Location p24 (191–210)
Author Location p24 (323–342 SF2)
Epitope VQNANPDCKTILKALGPAAT
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- Three of these 12 had CTL response to this peptide.
- The responding subjects were HLA-A3, A24, B8, B55; HLA-A1, A11, B8, B27.

HXB2 Location p24 (191–210)
Author Location p24 (323–342 SF2)
Epitope VQNANPDCKTILKALGPAAT
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location p24 (193–201)
Author Location Gag (327–335 SF2)
Epitope NANPDCKTI
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords inter-clade comparisons, rate of progression
References Tomiyama *et al.* 1999

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed.
- Four of the six epitopes were highly conserved among B subtype sequences, NANPDCKTI is conserved.

HXB2 Location p24 (193–201)
Author Location p24 (193–201)
Epitope NANPDCKTI
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Donor MHC A0201/31, B27/5101, Cw2; A2402/26, B7/5101, Cw7
Country Japan.
Assay type Chromium-release assay
Keywords epitope processing, escape
References Yokomaku *et al.* 2004

- Epitope variants escaped from being killed by CTLs in an endogenous expression system although they were recognized when corresponding synthetic peptides were exogenously loaded onto the cells. Escape is thus probably due to changes that occur during the processing and the presentation of epitopes in infected cells.
- Epitope variant nSnpdckNi was not recognized when added exogenously or when processed endogenously, but the mutations were in anchor residues and presumably inhibited binding to B*5101.

HXB2 Location p24 (193–201)
Author Location p24 (325–333)
Epitope NANPDCKTI?
Immunogen HIV-1 infection
Species (MHC) human (B51)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 3/11 of the HLA A2+ individuals were HLA B51 and two of these responded to this epitope as well as to other epitopes.

HXB2 Location p24 (193–201)
Author Location p24 (324–335 IIIB)
Epitope NANPDCKTI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope.

HXB2 Location p24 (193–201)
Author Location p24 (323–333)
Epitope NANPDCKTI
Epitope name NAN
Immunogen HIV-1 infection
Species (MHC) human (B51)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- None of the 8 study subjects recognized this epitope but none were HLA B51+

HXB2 Location p24 (193–201)
Author Location p24 (193–201)
Epitope NANPDCKTI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location p24 (193–201)
Author Location p24 (193–201)
Epitope NANPDSKTI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A*3101, A68, B*4403, B51
Keywords supervised treatment interruptions (STI)
References Arnedo-Valero *et al.* 2004

- T cell immune responses following STI were monitored in two chronically HIV-1 infected partners (A and B) who had contracted HIV-1 in 1992. STI induced strong transitory CD4+ and CD8+ T cell responses in both patients. Patient A displayed broad CD8+ T cell responses directed against Env, Pol, Gag, and Nef HIV-1 antigens. CTL responses in patient B were directed against two epitopes: Gag(p24)NANPDSKTI and Pol(RT)EELRQHLLRW.

HXB2 Location p24 (193–201)
Author Location p24 (191–205)
Epitope NANPDCKTI
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (194–202)
Author Location p24 (194–202)
Epitope ANPDCKTIL
Epitope name ANP
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This was one of 8 reactive epitopes found not to vary over time.

HXB2 Location p24 (195–202)
Author Location p24 (323–342)
Epitope NPDCKTIL
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Bernard *et al.* 1998

- This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population.
- No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs.
- Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XPXXXXXL is a B35 binding motif.

HXB2 Location p24 (195–202)
Author Location
Epitope NPDCKTIL
Epitope name Gag-NL8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B35, 3/17 (18%) recognized this epitope.

HXB2 Location p24 (197–205)
Author Location p24 (329–337 LAI)

Epitope DCKTILKAL
Subtype B
Immunogen
Species (MHC) human (B*0801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0801 epitope.

HXB2 Location p24 (197–205)
Author Location p24 (329–337 LAI)
Epitope DCKTILKAL
Subtype B
Immunogen
Species (MHC) human (B8)
References Sutton *et al.* 1993

- Predicted epitope based on B8-binding motifs, from larger peptide VQNANPDCKTILKAL.

HXB2 Location p24 (197–205)
Author Location p24 (329–337)
Epitope DCKTILKAL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords escape
References Nowak *et al.* 1995

- In a longitudinal study of CTL response and immune escape – the variant DCRTILKAL was also found, binds to B8, but is not recognized.

HXB2 Location p24 (197–205)
Author Location p24 (329–337)
Epitope DCKTILKAL
Immunogen
Species (MHC) human (B8)
References McAdam *et al.* 1995

- Defined as minimal epitope by titration and binding studies.

HXB2 Location p24 (197–205)
Author Location p24 (197–205)
Epitope DCKTILKAL
Immunogen
Species (MHC) human (B8)
References Goulder *et al.* 1997g

- Included in a study of the B8 binding motif.

HXB2 Location p24 (197–205)
Author Location p24 (329–337)
Epitope DCKTILKAL
Epitope name DCK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- This epitope was recognized at a low level by only 1 of the 7/8 study subjects that were HLA B8.
- Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy.

HXB2 Location p24 (197–205)
Author Location p24 (197–205)
Epitope DCKTILKAL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (197–205)
Author Location p24 (197–205)
Epitope DCKTILKAL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Day *et al.* 2001

- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.

HXB2 Location p24 (197–205)
Author Location p24
Epitope DCKTILKAL
Epitope name DCK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location p24 (197–205)
Author Location Gag (329–337)
Epitope DCKTILKAL
Immunogen HIV-1 infection
Species (MHC) humanized rabbit (B8)
Donor MHC A03, A28, B07, B08

Country Canada.
Assay type proliferation, Chromium-release assay, Flow cytometric CTL assay
Keywords HAART, ART, memory cells, immune dysfunction
References Gamberg *et al.* 2004a

- HAART restores HIV specific immunity after advanced infection by increase of CD4+ and CD8+ T cell numbers after supression of viral replication. However, HIV specific CTLs emerged only with detectable viral replication breakthroughs and were short-lived while CD4+ T-cell responses remained compromised, suggesting failure of generating stable CD8+ memory T-cells in the absence of HIV-specific T-helper responses.

HXB2 Location p24 (197–205)
Author Location (B consensus)
Epitope DCKTILKAL
Epitope name DL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A01, A03, B08, B14, Cw7, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location p24 (199–218)
Author Location Gag (331–350)
Epitope KTILRALGPGATLEEMMTAC
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location p24 (203–211)
Author Location Gag (335–343 SUMA)
Epitope KALGPAATL
Epitope name Gag KL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location p24 (209–217)
Author Location Gag (341–)
Epitope ATLEEMMTA
Epitope name Gag341
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* p24 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder that did not induce CTL and CD8+ T-cell IFN gamma responses in mice, although responses were detected in 2/17 HIV+ HLA-A2 subjects.

HXB2 Location p24 (211–230)
Author Location p24 (345–364 SF2)
Epitope LEEMMTACQGVGGPGHKARV
Immunogen HIV-1 infection
Species (MHC) human

References van Baalen *et al.* 1993

- Gag CTL epitope precursor frequencies estimated, peptide mapping.

HXB2 Location p24 (211–230)
Author Location p24 (343–362 SF2)
Epitope LEEMMTACQGVGGPGHKARV
Immunogen HIV-1 infection
Species (MHC) human (B7)
References McAdam *et al.* 1998

HXB2 Location p24 (211–231)
Author Location p24 (343–362 SF2)
Epitope LEEMMTACQGVGGPGHKARVL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.
- One of these 12 had CTL response to this peptide.
- The responding subject was HLA-A1, A2, B50, B57.

HXB2 Location p24 (213–221)
Author Location Gag (345–)
Epitope EMMTACQGV
Epitope name Gag345
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced a response in 1/6 transgenic mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.

HXB2 Location p24 (217–227)
Author Location p24 (349–359 IIIB)
Epitope ACQGVGGPGHK
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*1101 epitope.

HXB2 Location p24 (217–227)
Author Location Gag (349–359)
Epitope ACQGVGGPGHK
Subtype B, CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords inter-clade comparisons, TCR usage
References Fukada *et al.* 2002

- Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals.
- ACQGVGGPGHK was found to elicit clade-specific responses in clade B (ACQGVGGPGHK is most common in clades A and B) and clade E (acqgvggpShk is most common and is also common in clades C and D). ACQGVGGPGHK was recognized by CTL from 4/5 B clade infected Japanese subjects, and acqgvggpShk from 3/7 E clade infected Thai subjects.
- The binding of the two variants to HLA A*1101 was almost identical, but bulk CTL generated from individuals did not cross-react with the cross-clade peptides, indicating the lack of cross-reactivity was due to TCR specificity.

HXB2 Location p24 (217–227)
Author Location Gag (349–359 SUMA)
Epitope ACQGVGGPGHK
Epitope name Gag AK11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*1103)
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location p24 (217–227)

Author Location p24 (349–359 IIIB)
Epitope ACQGVGGPGHK
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by three lab workers accidentally infected with HIV-1 IIIB.
- ACQGVGGPSHK, a variant found in HIV RF, was also recognized.

HXB2 Location p24 (217–227)
Author Location p24 (SF2)
Epitope ACQGVGGPGHK
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location p24 (217–227)
Author Location p24 (349–359)
Epitope ACQGVGGPGHK
Epitope name ACQ
Immunogen HIV-1 infection
Species (MHC) human (A11)
Donor MHC A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2/8; A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- Both of the 2/8 HLA-A11 study subjects recognized this CTL epitope.
- Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197.
- Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up.

HXB2 Location p24 (217–227)
Author Location p24 (216–226)
Epitope ACQGVGGPGHK
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location p24 (217–227)
Author Location p24 (349–359 SF2)
Epitope ACQGVGGPGHK
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 2/2 group 3.

HXB2 Location p24 (217–227)
Author Location p24
Epitope ACQGVGGPGHK
Epitope name ACQ
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).

- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location p24 (217–227)
Author Location (B consensus)
Epitope ACQGVGGPGHK
Epitope name AK11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
Donor MHC A11, A29, B08, B44, Cw4, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location p24 (221–231)
Author Location p24 (353–363 LAI)
Epitope VGGPGHKARVL
Epitope name G1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location p24 (223–231)
Author Location p24 (223–231 SF2)
Epitope GPGHKARVL
Epitope name GL9
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
References Altfeld *et al.* 2001a

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- The response to GPGHKARVL was dominant.

HXB2 Location p24 (223–231)
Author Location (C consensus)
Epitope GPSHKARVL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p24 (223–231)
Author Location p24 (355–363 LAI)
Epitope GPGHKARVL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords review, escape
References Goulder *et al.* 1997e; Goulder *et al.* 1997a

- HLA-identical sibling hemophiliac brothers were both infected with the same batch of factor VIII.
- One had a strong response to this peptide, the other a weak response. They were tested 6-8 years after infection.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location p24 (223–231)
Author Location p24 (SF2)
Epitope GPSHKARVL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.

- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location p24 (223–231)
Author Location p24 (SF2)
Epitope GPSHKARVL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location p24 (223–231)
Author Location (LAI)
Epitope GPGHKARVL
Subtype B
Immunogen
Species (MHC) (B7)
Keywords optimal epitope
References Frahm *et al.* 2004; Goulder 1999

HXB2 Location p24 (223–231)
Author Location p24 (223–231 SF2)
Epitope GPGHKARVL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 1/4 group 1, 2/3 group 2, and 0/1 group 3.

HXB2 Location p24 (223–231)
Author Location p24 (223–231)
Epitope GPGHKARVL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location p24 (223–231)
Author Location p24 (223–231)
Epitope GPGHKARVL
Epitope name B7-GL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), immunodominance, acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- Only two epitopes were detected during acute infection in patient AC-06, B7 restricted gp41 epitope IPRRIRQGL and Gag GPGHKARVL. GPGHKARVL was the first targeted peptide, and remained immunodominant through the 34 month study period.
- 3/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.

HXB2 Location p24 (223–231)
Author Location p24 (223–231)
Epitope GPGHKARVL
Epitope name B7-GL9 Gag
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the intial CTL response.
- In the earliest sample at day18 the sequence for this epitope was gpShkarvl. gpghkarvl dominated at day 606; both were equally well recognized.
- This was an immunodominant epitope, and was present in both viruses, the original strain and the superinfecting strain.

HXB2 Location p24 (223–231)
Author Location p24 (223–231)
Epitope GPGHKARVL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 4/7 patients recognized this epitope.

HXB2 Location p24 (223–231)
Author Location (B consensus)
Epitope GPGHKARVL
Epitope name GL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, B07, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location p24
Author Location p24
Epitope EELRQHLLRW
Immunogen HIV-1 infection
Species (MHC) human (B44)
Donor MHC A01, A32, B*1410, B15; A*3101, A68, B*4403, B51
Country Spain.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HAART, ART, supervised treatment interruptions (STI)
References Arnedo-Valero *et al.* 2004

- T cell immune responses following STI were monitored in two chronically HIV-1 infected partners (A and B) who had contracted HIV-1 during 1992. STI induced strong transitory CD4+ and CD8+ T cell responses in both patients. The viruses remained very closely related over 10 years, despite the two individuals having different HLA types; the authors suggest the maintained similarity does not support a strong role for HLA driven HIV diversity as has been claimed in Moore et al. (Science 2002).
- During the second treatment stop, patient A developed a strong proliferative response to p24, and multiple strong CD8+ T cell repsonses to Env, Pol, Gag and Nef. This patient was able to control viral load for two years follow up without therapy. Patient B developed a very weak CD4+ T cell response against p24 during breaks in therapy, and had CD8+ responses to two epitopes. Patient A: A01, A32, B*1410, B15; Patient B: A*3101, A68, B*4403, B51.

HXB2 Location p24
Author Location p24
Epitope NANPDCKTI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A01, A32, B*1410, B15; A*3101, A68, B*4403, B51
Country Spain.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HAART, ART, supervised treatment interruptions (STI)
References Arnedo-Valero *et al.* 2004

- T cell immune responses following STI were monitored in two chronically HIV-1 infected partners (A and B) who had contracted HIV-1 during 1992. STI induced strong transitory CD4+ and CD8+ T cell responses in both patients. The viruses remained very closely related over 10 years, despite the two individuals having different HLA types; the authors suggest the maintained similarity does not support a strong role for

HLA driven HIV diversity as has been claimed in Moore et al. (Science 2002).
- During the second treatment stop, patient A developed a strong proliferative response to p24, and multiple strong CD8+ T cell repsonses to Env, Pol, Gag and Nef. This patient was able to control viral load for two years follow up without therapy. Patient B developed a very weak CD4+ T cell response against p24 during breaks in therapy, and had CD8+ responses to two epitopes. Patient A: A01, A32, B*1410, B15; Patient B: A*3101, A68, B*4403, B51.

II-B-4 Gag p24-p2p7p1p6 CTL, CD8+, epitopes

HXB2 Location p24-p2p7p1p6 (223–1)
Author Location Gag
Epitope GPGHKARVLA
Immunogen
Species (MHC) human (B7)
References De Groot *et al.* 2001
- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay.
- GPGHKARVLA was confirmed as an HLA-B7 epitope in this study, and had been previously published.

HXB2 Location p24-p2p7p1p6 (223–1)
Author Location Gag
Epitope GPGHKARVLA
Epitope name 1291
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, A24, B07, B38, Cw07, Cw12/13; A01, A03, B07, B08, Cw03, Cw07
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003
- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for GPGHKARVLA: 28%

HXB2 Location p24-p2p7p1p6 (225–8)
Author Location Gag (357–372 LAI)
Epitope GHKARVLAEATLSQVN
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Buseyne *et al.* 1993a
- Vertical transmission of HIV ranges from 13% to 39%.
- Primary assays showed that cytotoxic activity against at least one HIV protein was detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag.

HXB2 Location p24-p2p7p1p6 (230–7)
Author Location Gag (386–)
Epitope VLAEAMSQV
Epitope name Gag-386
Immunogen
Species (MHC) human (A*0201)
Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction, immunodominance
References Altfeld *et al.* 2001c
- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- VLAEAMSQV binds to all five HLA-A2 supertype alleles tested: A*0201, A*0202, A*0203, A*0206 and A*6802 (highest affinity)
- 4/22 individuals with chronic HIV-1 infection recognized this epitope, and it was immunodominant in 3/4 by ELISPOT.
- 0/12 acutely infected individuals recognized this epitope.

HXB2 Location p24-p2p7p1p6 (230–7)
Author Location Gag
Epitope VLAEAMSQV
Epitope name Gag 386
Subtype M
Immunogen Vaccine, in vitro stimulation or selection, computer prediction
Vector/Type: DNA, peptide *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, mouse, humanized mouse (A*0201)
Assay type cytokine production, T-cell Elispot
Keywords inter-clade comparisons, computational epitope prediction, escape, TCR usage, variant cross-recognition or cross-neutralization
References McKinney *et al.* 2004
- This study examined variant recognition of epitopes presented by A*0201 and A*1101. Numerous amino acid substitutions can be introduced into epitopes without disrupting their recognition by CTLs, although epitopes with multiple substitutions were less recognized. An algorithm was constructed for prediction of epitopes capable of inducing responses to a great number of variant epitopes.

- A total of 20 variant forms of Gag 386 were identified. More than 95% of the variant epitopes were recognized by CTLs from mice immunized with the parental form.
- Gag 386 epitope (parent or variant form) was present in 97% of HIV sequences of many M group subtypes.

HXB2 Location p24-p2p7p1p6 (230–7)
Author Location
Epitope VLAEAMSQV
Epitope name Gag-VV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A02, 3/29 (10%) recognized this epitope.

HXB2 Location p24-p2p7p1p6 (230–7)
Author Location Gag (362–)
Epitope VLAEAMSQV
Epitope name Gag362(9L)
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type T-cell Elispot, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.
- The variant vlaeamsqA was also immunogenic in A2 transgenic mice, eliciting a CD8+ T-cell response, as was recognized in 3/17 HIV+ people, including the person that recognized the vlaeamsqV variant.

HXB2 Location p24-p2p7p1p6 (230–7)
Author Location Gag (397–405)
Epitope VLAEAMSQV
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)

II-B-5 Gag p2p7p1p6 CTL, CD8+, epitopes

HXB2 Location p2p7p1p6 (1–10)
Author Location p2p7p1p6 (1–10)
Epitope AEAMSQVTNS
Immunogen
Species (MHC) human (B*4501)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p2p7p1p6 (5–13)
Author Location Gag (SF2)
Epitope SQVTNPANI
Immunogen Vaccine
Strain: B clade SF2 *HIV component:* Gag
Species (MHC) mouse (H-2D^{b})
References Paliard *et al.* 1998

- HIV-1 (SF2)p55gag vaccination of H-2 mice activates a CTL response against this epitope.
- CTL that recognized SQVTNPANI in the context of H-2D^{b} cross-reacted with H-2 alloantigens H-2L^{d} and an unidentified self-peptide.
- A postulate: heterozygosity at the MHC level could prevent the maturation of some T cell receptor combinations for foreign peptide and self-MHC constructs because of thymic depletion and tolerance.

HXB2 Location p2p7p1p6 (18–37)
Author Location Gag (96ZM651.8)
Epitope SNFKGNKRMVKCFNCGKEGH
Immunogen
Species (MHC) human (A*02011)
References Novitsky *et al.* 2001

- This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort.
- 4 of 8 individuals (50%) who were positive for HLA-A*02011 responded to the peptide SNFKGNKRMVKCFNCGKEGH.

HXB2 Location p2p7p1p6 (38–47)
Author Location Gag
Epitope LARNCRAPRK
Epitope name 1331
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A23, B49, B57, C?; A03, A24, B27, B57, Cw13, Cw18; A03, A26, B08, B52, ?
Country United States.
Assay type T-cell Elispot

Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for LARNCRAPRK: 35%. Immunodominant epitope.

HXB2 Location p2p7p1p6 (42–50)
Author Location p15 (42–50)
Epitope CRAPRKKGC
Immunogen HIV-1 infection
Species (MHC) human (B*14)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p2p7p1p6 (42–50)
Author Location p15 (42–50 SF2)
Epitope CRAPRKKGC
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Donor MHC B14
Keywords immunodominance
References Yu *et al.* 2002b

- 26/57 HIV-1 infected subjects displayed Gag p15-specific CD8+ T-cell IFNgamma responses were measured by Elispot and intracellular staining. The immunodominant regions targeted by CD8+ T-cells were mapped to three functional domains: the zinc finger structures, the protease cleavage site p7/p1, and to the Vpr binding site in p6.
- p15 contributed on average 17% of the total Gag response (rage 0-100%).
- 3 optimal CTL epitopes were mapped within p15: KELYPLTSL, CRAPRKKGC, and FLGKIWPSYK.
- 2/6 HLA-B14+ subjects recognized this epitope. The binding motif for B14 is C-term Cys, positions 2 and 5 Arg.

HXB2 Location p2p7p1p6 (42–50)
Author Location (B consensus)
Epitope CRAPRKKGC
Epitope name CC9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Donor MHC A28, A29, B14, B44, Cw8
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope

HXB2 Location p2p7p1p6 (55–70)
Author Location p15 (446–460 BRU)
Epitope KEGHQMKDCTERQANF
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Claverie *et al.* 1988

- One of 4 epitopes first predicted, then subsequently shown to stimulate an HLA-A2 restricted CTL line.

HXB2 Location p2p7p1p6 (55–70)
Author Location Gag (41–56)
Epitope KEGHQMKDCTERQANF
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 19 patients recognized this epitope.

HXB2 Location p2p7p1p6 (63–71)
Author Location p15 (63–71)
Epitope CTERQANFL
Immunogen HIV-1 infection
Species (MHC) human (B61)
Donor MHC A*0201, A11, B51, B61, Cw2, Cw14
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.

- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location p2p7p1p6 (64–71)
Author Location
Epitope TERQANFL
Epitope name Gag-TL8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Donor MHC A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- This epitope was newly defined in this study.
- Patient 01RCH59 was Hispanic, not on HAART, and had a viral load of 5100 and CD4 count of 349 – she also recognized AEWDRVHPV, p24(78-86), HLA-B*4002 and KEKGGLEGL, Nef(92-100), HLA-B*4002.
- Among HIV+ individuals who carried HLA B40, 3/5 (60%) recognized this epitope.

HXB2 Location p2p7p1p6 (64–71)
Author Location p15 (64–71)
Epitope TERQANFL
Immunogen
Species (MHC) human (B*4002)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p2p7p1p6 (66–80)
Author Location p15 (66–80)
Epitope RQANFLGKIWPSYKG
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location p2p7p1p6 (70–77)
Author Location Gag (433–)
Epitope FLGKIWPS
Epitope name Gag433
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 7/17 HIV+ HLA-A2 subjects.

HXB2 Location p2p7p1p6 (70–79)
Author Location p15 (70–79 SF2)
Epitope FLGKIWPSYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords immunodominance
References Yu *et al.* 2002b

- 26/57 HIV-1 infected subjects displayed Gag p15-specific CD8+ T-cell IFNgamma responses were measured by Elispot and intracellular staining. The immunodominant regions targeted by CD8+ T-cells were mapped to three functional domains: the zinc finger structures, the protease cleavage site p7/p1, and to the Vpr binding site in p6.
- p15 contributed on average 17% of the total Gag response (rage 0-100%).
- 3 optimal CTL epitopes were mapped within p15: KELYPLTSL, CRAPRKKGC, and FLGKIWPSYK.

- FLGKIWPSYK was embedded in a peptide recognized by 14/57 (25%) of subjects.
- 13/24 (54%) of HLA-A*0201+ subjects recognized this peptide.

HXB2 Location p2p7p1p6 (70–79)
Author Location p2p7p1p6 (1–10)
Epitope FLGKIWPSYK
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p2p7p1p6 (70–79)
Author Location (C consensus)
Epitope FLGKIWPSHK
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location p2p7p1p6 (83–97)
Author Location Gag (453–462 BH10, LAI)
Epitope GNFLQSRPEPTAPPF
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is PEPTAPPFLQ) has similarity with the T-cell surface glycoprotein CD5, fragment PEPTAPPRLQ.

HXB2 Location p2p7p1p6 (83–97)
Author Location p15 (418–433 BRU)
Epitope GNFLQSRPEPTAPPF
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Claverie *et al.* 1988

- One of 4 epitopes first predicted, then subsequently shown to stimulate an HLA-A2 restricted CTL line.

HXB2 Location p2p7p1p6 (83–97)
Author Location Gag (69–83)
Epitope GNFLQSRPTAPPF
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 19 patients recognized this epitope.

HXB2 Location p2p7p1p6 (118–126)
Author Location p2p7p1p6 (33–41)
Epitope KELYPLTSL
Immunogen HIV-1 infection
Species (MHC) human (B*4001)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location p2p7p1p6 (118–126)
Author Location p2p7p1p6 (118–126)
Epitope KELYPLTSL
Immunogen
Species (MHC) human (B*4001(B60))
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes that this is a B*4001 epitope.

HXB2 Location p2p7p1p6 (118–126)
Author Location p15 (118–126 SF2)
Epitope KELYPLTSL
Epitope name p15-24
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B60, B*4001)
Keywords immunodominance, cross-presentation by different HLA
References Yu *et al.* 2002b

- 26/57 HIV-1 infected subjects displayed Gag p15-specific CD8+ T-cell IFNgamma responses were measured by Elispot and intracellular staining. The immunodominant regions targeted by CD8+ T cells were mapped to three functional domains: the zinc finger structures, the protease cleavage site p7/p1, and to the Vpr binding site in p6.
- p15 contributed on average 17% of the total Gag response (rage 0-100%).
- 3 optimal CTL epitopes were mapped within p15: KELYPLTSL, CRAPRKKGC, and FLGKIWPSYK.
- Four patients who were HLA-B60+ recognized KELYPLTSL.
- The binding motif for B60 is C-term Leu and 2nd position Glu.
- Four patients who did not carry HLA-B60 also recognized the 15 amino acid long peptide carrying KELYPLTSL, suggesting other epitopes in this immediate region can be presented by other HLA class I molecules.

HXB2 Location p2p7p1p6 (121–129)
Author Location p2p7p1p6 (36–44)
Epitope YPLASLRSL
Epitope name B7-YL9 Gag
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant ypPlaslrsl. The CTL response was zero at all timepoints for the first variant. Insertion of a proline at position 3 (first variant) resulted in prevention of initial presentation of this region to the immune system.

HXB2 Location p2p7p1p6 (121–130)
Author Location Gag (484–493)
Epitope YPLTSLRSLF
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Jin *et al.* 2000b

- This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor.
- A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing.

II-B-6 Gag CTL, CD8+, epitopes

HXB2 Location Gag
Author Location Gag (IIIB)
Epitope
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* Gag
Species (MHC) macaque
References Paliard *et al.* 2000

- CTLs primed by HIV-1 p55 gag virus-like particle (VLP) vaccination recognized epitopes in four different 20 amino acid peptides p17/4, p17/8, p24/13 and p14/9.
- Cytotoxic T cell response lasted greater than 8.5 months.

HXB2 Location Gag
Author Location Gag (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1
References Wasik *et al.* 2000

- HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of beta-chemokines and IL-2 relative to other HIV+ infants.
- HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors.
- CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs.

HXB2 Location Gag
Author Location Gag (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp41, Protease, V3
Species (MHC) human
References Salmon-Ceron *et al.* 1999

- The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36))
- Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36.
- Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* p17 Gag, p24 Gag
Species (MHC) human
References Klein *et al.* 1997

- Immunization of HIV+ people with an HIV-1 p17/p24 Ty virus-like particle (p24-VLP) resulted in a marginal, short-lived increased proliferative response to p24 and p17 and a transient elevation in viral load.
- Two of four subjects that received 500 or 1000 μg of p24-VLP had an increase in gag-specific CTL.

HXB2 Location Gag
Author Location p24 (SF2)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade SF2 *HIV component:* gp120, p24 Gag *Adjuvant:* MF59, PLG
Species (MHC) mouse, baboon
References O'Hagan *et al.* 2000

- PLG (Polylactide co-glycolide polymer) microparticles administered in MF59 emulsion induced gp120 Ab responses and CTL immune responses against p24 gag.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Lubaki *et al.* 1999

- Three strategies were used to analyze CTL activity: area under the net HIV-specific lysis curve (ACU), linear regression (LR) of net specific lysis, and the standard method, lytic units (LU20)
- A correlation between low HIV plasma viral load and increased levels of HIV-specific Gag and Nef CTL activity was observed using ACU and LR, but not LU20.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Kalams *et al.* 1999a

- The presence of HIV-1 p24-specific proliferative responses was positively correlated with Gag-specific memory CTL and negatively correlated with viral load in untreated subjects.
- Gag proliferative responses were the most readily detected – Gag CTL responses were the only responses with a significant correlation with Gag stimulated help, although there was a positive trend with Nef, Env and RT.

HXB2 Location Gag
Author Location p55 (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Greenough *et al.* 1999

- 7/128 HIV-1 infected hemophiliac were identified as long-term non-progressors (LTNPs) and were monitored for viral and host immune parameters over 15 years – LTNPs maintained a low viral load, high frequencies of CTL precursors directed against Gag antigen and low levels of HIV-specific effector CTL activity – effector cell activity suggests low level ongoing viral replication.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Trickett *et al.* 1998

- Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection.
- Improvement in CD4+ and CD8+ T cells was seen in 7/12, and an increase in the CTL response to Gag was seen in one patient.

HXB2 Location Gag
Author Location Gag (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Betts *et al.* 1999

- This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection.

HXB2 Location Gag
Author Location Gag (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Legrand *et al.* 1997

- Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat.
- An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef.
- Early responses to Pol, Rev, Vif and Tat were rare.

HXB2 Location Gag
Author Location Gag (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Betts *et al.* 1997

- 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins.
- A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References De Maria *et al.* 1997

- CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function.
- Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels.

HXB2 Location Gag
Author Location Gag (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Protease
Species (MHC) human
References Belshe *et al.* 1998

- The live canarypox vaccine ALVAC-HIV(vCP205) carrying MN gp120, LAI gp41, Gag and Protease, and boosted with SF-2 rpg120, was given to HIV-1 seronegative volunteers – HIV-specific Env or Gag CD8+ CTL were detected in 64% of the volunteers.

HXB2 Location Gag
Author Location Gag (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Buseyne *et al.* 1998a

- This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load.

HXB2 Location Gag
Author Location Gag (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Buseyne *et al.* 1998b

- In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human
References Goh *et al.* 1999

- 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype.
- In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins.

HXB2 Location Gag
Author Location Gag (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: canarypox *HIV component:* Gag, gp120, gp41, Nef, Protease, RT
Species (MHC) human
References Evans *et al.* 1999

- A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination.

HXB2 Location Gag
Author Location p17
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing
References Kuiken *et al.* 1999

- A correlation between conserved regions of p17 or Nef and CTL epitope density was noted – the authors suggest that this may be due to a biological reason such as epitope processing, or may possibly be an artifact of experimental strategy for epitope definition such that conserved epitopes would tend to be identified because they would be more likely to be cross-reactive with the test reagents.
- In contrast to p17 and Nef, p24 is a more conserved protein and known epitopes are evenly distributed across p24.

HXB2 Location Gag
Author Location Gag (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA prime with vaccinia boost *Strain:* B clade LAI *HIV component:* Env, Gag
Species (MHC) macaque
Keywords Th1, Th2
References Kent *et al.* 1998

- Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T cell immunity than either vaccine alone.
- The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced.

HXB2 Location Gag
Author Location Gag/Pol (LAI, MN)
Epitope
Immunogen Vaccine
Vector/Type: canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease
Species (MHC) human
References Salmon-Ceron *et al.* 1999

- A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy, uninfected volunteers.

HXB2 Location Gag
Author Location Gag/Pol (MN)
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86
Species (MHC) chimpanzee
References Kim *et al.* 1998

- The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.

HXB2 Location Gag
Author Location Gag (BRU)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Aladdin *et al.* 1999

- *In vitro* measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death.

HXB2 Location Gag
Author Location p24 (C consensus)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, immunodominance
References Goulder *et al.* 2000a

- The CTL-dominant response was focused on this epitope in a HIV+ South African – this epitope did not fall within the five most recognized peptides in the study.
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* ZF1 *HIV component:* complete genome
Species (MHC) macaque
References Akahata *et al.* 2000

- Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging.
- Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153)
- 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected.
- PBMC from all vaccinated monkeys produced IFN-gamma, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response.
- 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit.
- 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Salerno-Goncalves *et al.* 2000

- A general test of CD8 anti-viral activity was developed based on proviral load of coculture of autologous CD8+ cells with CD4+ cells after homogeneous superinfection with NSI virus.
- Significantly decreased the CD4+ T-cell proviral loads were found in 12 HIV+ slow progressors relative to 10 rapid progressors.
- Significant CD8+ mediated cytotoxicity directed against autologous cells infected with vaccinia carrying the HIV-1 gag gene was observed in slow progressors in contrast to rapid progressors, but no correlation was found between plasma viral load in 22/22 asymptomatic HIV infected individuals.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Young *et al.* 2001

- Addition of recombinant rec human IL12 (rhIL12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/ul > 500.
- 2/10 individuals with <200 CD4 cells/ul, and 3/10 individuals with 200-500 CD4cells/ul, had an increase of >5% upon treatment of the culture with rhIL12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL12.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) mouse
References de Quiros *et al.* 2000

- CB-17 SCID-Hu mice engrafted with peripheral blood mononuclear cells of four long-term nonprogressors (viral load < 50 copies/ml) displayed resistance to challenge with HIV-1 SF162, mediated by CD8+ T-cells and associated with proliferation in response to p24 – these patients did not have a higher level of HIV-1 specific immunity *in vitro*, so the mechanism is unknown.

HXB2 Location Gag
Author Location Gag (subtype A, B, D)
Epitope

Subtype A, B, D
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Cao *et al.* 2000

- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, RT or Nef from HIV-1 clades A, B, and D.
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References White *et al.* 2001

- HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women.

HXB2 Location Gag
Author Location Gag (HXB2)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Chun *et al.* 2001

- Suppression of viral replication in the resting CD4+ T-cell reservoir by autologous CD8+ T-cells via CD4+/CD8+ cell contacts was observed in long-term nonprogressors and patients undergoing antiretroviral treatment, but this activity appears to be independent of Gag-specific CTL activity.

HXB2 Location Gag
Author Location Gag (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Jin *et al.* 2000a

- The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets.
- LTNPs have high memory CTL numbers and low viral load.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Keywords review, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 2001

- This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population.
- The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays.
- CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases.
- CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response.
- HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people.

HXB2 Location Gag
Author Location
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol
Species (MHC) mouse
Keywords review, vaccine-specific epitope characteristics
References Nabel 2002

- Using DNA that had humanized codon usage, CTL responses to DNA vaccines containing either Gag, Pol, Gag-Pol fusion protein, or Gag-Pol pseudoparticles suggested that the greatest breadth and most potent response was to the Gag-Pol fusion protein. The Gag-Pol fusion lacks the Gag precursor protein required for viral assemble, so does not form releaseable particles; the author speculates that longer retention of the Gag-Pol protein with in the cell may enhance antigen presentation.

HXB2 Location Gag
Author Location
Epitope
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References De Maria *et al.* 1994; Kuhn *et al.* 2002

- 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Gag
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References Aldhous *et al.* 1994; Kuhn *et al.* 2002

- Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points.
- Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses to Tat (1/2), Pol (2/2), Gag (1/2).
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Gag
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission, rate of progression
References Kuhn *et al.* 2002; Wasik *et al.* 1999

- In HIV-infected infants HIV-specific, CTL responses were not detectable in icord blood or in PBMC collected shortly after birth and were absent or remained very low in 3 infants with a rapidly progressive disease. For those who progressed more slowly, the HIV-specific CTL activity varied.
- The two infants with high levels of Env peptide-stimulated IL-2 responses had the highest CTLp frequencies.
- Stronger responses were detected after initiation of the antiretroviral therapy.
- Two babies that were not infected though born to HIV+ mothers had detectable though low HIV-specific CTLp responses to Env (1/2), Pol (2/2), Gag (1/2) cord blood and transiently in PBMC after birth.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Gag
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References Kuhn *et al.* 2002; McFarland *et al.* 1994

- Only 9% of HIV+ infants had HIV-specific CTL against Env or Gag in unstimulated PBMC. After CD3 stimulation of PBMC, Gag and Env specific CTL were found in PBMC from 91% and 78% of HIV-infected children, respectively, with high precursor frequencies.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Gag
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. p17 is much more variable than p24.

HXB2 Location Gag
Author Location p24 (HXB)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, vaccine-specific epitope characteristics
References Lu *et al.* 2000a

- Bacillus anthrax lethal toxin (LFn)-HIV fusion proteins are candidate HIV vaccines that are safe in mice, and LFn-V3 region fusion proteins induce CD8 T cells in BALBc mice. LFn causes exogenous protein to be taken up and processed in a class I pathway. Expressed proteins from Gag p24 and Nef fragments cloned into the LFn expression plasmid stimulate gag-specific CD4 proliferation and CTL responses in HIV-infected donor PBMCs *in vitro*.

HXB2 Location Gag
Author Location (HXB2)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Edwards *et al.* 2002

- 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag.
- Nef and/or Pol CTL responses were detected in 86% of the subjects.
- The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load.
- Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count.
- Nef and Env responses did not correlate with either CD4 counts or viral load.

HXB2 Location Gag
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, dendritic cells
References Larsson *et al.* 2002b

- Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.

HXB2 Location Gag
Author Location (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunotherapy
References Trickett *et al.* 2002

- Conditions were optimized for ex-vivo expansion of CD8+ and CD4+ T-cells with the goal of functional T-cell production for autologous immunotherapy. 10,000-fold expansions were obtained in 14 days with optimized concentrations of IL-2, anti-CD3 and anti-CD28 coated microspheres, and decreasing amounts of serum over the first 8 days.

HXB2 Location Gag
Author Location (IIIB)
Epitope
Subtype B
Immunogen HIV-1 and HCV co-infection
Species (MHC) human
Keywords rate of progression
References Lauer *et al.* 2002

- HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins.
- All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load.
- Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted.
- HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.

HXB2 Location Gag
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords responses in children
References Luzuriaga *et al.* 1995

- 2/3 infants infected in utero had detectable HIV-1 Gag and Env specific CTL responses, one by 4 months, one by 11 months of age. Levels of the responses varied at different time point. Pol responses were not detected.
- 2/4 infants infected intrapartum had detectable responses, one note until 11 months, one not until 42 months.
- HIV-specific CTL were not detected in ten HIV- infants that were born to HIV+ mothers.

HXB2 Location Gag
Author Location
Epitope
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN *HIV component:* Env, Gag
Species (MHC) human
References Gupta *et al.* 2002

- Different HIV strains were used for different regions: Gag, LAI; gp120, MN; and gp41, LAI
- A safety and immunogeniticity study of a vaccine dosing schedule was studied in a trial conducted in high and low risk study subjects. There was a 76% cumulative probability of detecting a Gag or Env CTL response by day 728.

HXB2 Location Gag
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, responses in children
References Scott *et al.* 2001

- CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age.
- Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses.
- One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol.
- Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.

HXB2 Location Gag
Author Location (IIIB, MN)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords dendritic cells
References Larsson *et al.* 2002a

- Dendritic cells acquire and present HIV-1 antigens derived from dead, apoptotic cells or from non-infectious, fusion-competent HIV-1 virions, and these DC cells could stimulate CD4+ and CD8+ T-cells resulting in IFNgamma production in an Elispot assay. Both HLA Class I and class II molecules were used for presentation. This may be an important aspect of the initial immune response to HIV-1 infection of CD4+ cells in the mucosal subepithelia.

HXB2 Location Gag
Author Location (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, supervised treatment interruptions (STI)
References Ortiz *et al.* 2001

- Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.

HXB2 Location Gag
Author Location Gag
Epitope
Subtype AG, B
Immunogen
Species (MHC) human
References

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen
Species (MHC) human
References

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type Intracellular cytokine staining
Keywords HAART, ART, computational epitope prediction, supervised treatment interruptions (STI)
References Amicosante *et al.* 2002

- A new assay was developed to detect CTL responses to HIV using 28 pooled 15-mer peptides from conserved regions in Gag that were selected to be rich in HLA class I motifs, carrying potential epitopes for more than 90% of HLA class I haplotypes, and to be conserved between subtypes. Some peptide variants were included, expanding the potential for cross-clade recognition. 12 Caucasians, even those on successful HAART, had detectable CTL responses using this assay, and as did five Africans. People with either B subtype or A-G recombinant infections all reacted.
- The Gag peptide ICS assay was more sensitive to picking up CTL reactivity than whole Gag in HAART treated people. Initiation of STI increased the number of IFN-gamma producing CD8+ T-cells detected using the peptide assay.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* Gag
Adjuvant: block copolymer CRL8623
Species (MHC) macaque
Assay type CD8 T-cell Elispot - IFNγ
Keywords vaccine-induced epitopes
References Caulfield *et al.* 2002

- Codon-optimized HIV Gag DNA vaccines were given i.m. with or without a nonionic block copolymer(CRL8623) as adjuvant. DNA-CRL8623 fourmulations induced 2-fold higher Elispot responses, shifting the response towards CD8+ T-cells.
- 23 monkeys recognized 25 different epitopes with an average of 2.7 epitopes per monkey, and a minimum of 1 and a maximum of 5 peptides per monkey.
- Responses were detected up to 18 months after vaccination.

HXB2 Location Gag
Author Location Gag
Epitope
Subtype multiple
Immunogen
Species (MHC) human
Assay type Flow cytometric CTL assay
Keywords inter-clade comparisons
References Currier *et al.* 2003

- CD8-cellular immune responses from 21 HIV-1 infected patients from Kenya infected with subtype A, C, D, and unique recombinants were studied for cross-recognition of Gag, Env, and Nef vaccinia-expressed proteins representing subtypes A-H, including CRF01.
- Both subtype-specific and cross-reactive CTL were observed, with a skewing of responses towards the infecting subtype in the nine subjects with full length sequence available. The magnitude of the responses to Gag were the highest, less to Nef, and still less to Env.
- For Gag, 8/21 subjects responded to at least 7/8 different subtype proteins, 7 had a mixed response, recognizing some subtypes but not others, and 6 responded to only one or none of the different subtype proteins. For Env, 4/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 7 responded to one or none. For Nef, 5/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 6 responded to one or none.

HXB2 Location Gag
Author Location Gag (SF2)
Epitope
Subtype B
Immunogen Vaccine

Vector/Type: DNA, protein, virus-like particle (VLP), PLG microparticle *Strain:* B clade SF2 *HIV component:* Gag *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72), LTK63
Species (MHC) macaque
Assay type proliferation, Chromium-release assay
References Otten *et al.* 2003

- Immunization strategies for Gag (p55) in macaques were compared. GAG DNA prime with a boost of Gag adsorbed onto PLG (polyactide coglycolide) microparticles with LTK63 as adjuvant gave the strongest CD4+ T cell proliferative, CTL, and antibody responses, compared with Gag protein, or Gag virus-like particles (VLP). GAG DNA was best for inducing CTL responses, Gag-PLG for T-help and antibody; the prime-boost combination gave strong responses for all three.

HXB2 Location Gag
Author Location Gag
Epitope
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords rate of progression, immunodominance, acute infection, early-expressed proteins
References Masemola *et al.* 2004a

- Anti-HIV T-cell responses in subtype C HIV-1 infected individuals in the beginning of the infection target multiple protein regions, but the responses are dominated by Nef, making up almost one-third of the total responses; the second most targeted protein was p24. A correlation between Gag specific responses and plasma viral load was also found.
- Neither breadth nor magnitude of CD8+ T-cell responses were correlated with control of virus, however hierarchical preferential targeting of Gag was significantly associated with lower viral loads.

HXB2 Location Gag
Author Location Gag
Epitope
Subtype A
Immunogen Vaccine
Vector/Type: DNA, modified vaccinia Ankara (MVA), polyepitope, DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17/p24 Gag
Species (MHC) human
Country United Kingdom.
Assay type CD8 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine-induced epitopes, vaccine antigen design
References Mwau *et al.* 2004

- Phase I clinical trial in healthy uninfected individuals was conducted evaluating the immunogenicities of candidate DNA- and MVA-vectored HIV vaccines. Both DNA and MVA vaccines alone and combined (DNA prime-MVA boost) were shown to be safe and induce HIV-specific responses in 78%, 88% and 89% of individuals, respectively. Responses in some individuals could be detected 1 year after vaccination.
- The vaccine in this case was a clade A p17/p24 antigen linked to a polyepitope string of A clade eptiopes. Reponses were tested with peptide pools, and multiple strong responses to the gag proteins and to the poylepitope region were observed. MVA alone did as well as a DNA prime, MVA boost in this study, although the study included small numbers.

HXB2 Location Gag
Author Location Gag
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: non-replicating adenovirus *Strain:* B clade *HIV component:* Gag
Species (MHC) mouse
Assay type Intracellular cytokine staining
Keywords Th1, Th2
References Pinto *et al.* 2003

- Heterologous prime boosts with replication-defective adenoviral vectors of different simian serotypes expressing the same transgene product of HIV-1 were shown to be highly efficient in increasing specific CD8+ T-cell responses.

HXB2 Location Gag
Author Location
Epitope
Immunogen computer prediction
Species (MHC) (A*0201, B*3501)
Keywords inter-clade comparisons, computational epitope prediction
References Schönbach *et al.* 2002

- Computational methods (artificial neural networks, hidden Markov models, binding matrices based on HLA association rates) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human (A*0201, Cw*08)
References Shacklett *et al.* 2000

- HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples.

HXB2 Location Gag
Author Location Gag
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*35)
Keywords rate of progression

References Jin *et al.* 2002

- Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501.
- Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env.
- The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.

HXB2 Location Gag
Author Location
Epitope
Subtype A, B, C
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost, canarypox prime with gp160 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Nef, Pol
Species (MHC) human (B60)
Keywords inter-clade comparisons, vaccine-specific epitope characteristics
References Ferrari *et al.* 2001

- Different HIV strains were used for different regions: gp41 LAI, Gag LAI, gp120 MN, gp120 SF2
- HLA-B60 responses dominated the responses against an Gag vaccine in an individual (022G0Z) who was HLA A1, A11, B8, B60. The strongest response was against the MN peptide 107-136. Low level Gag responses were observed against B8 and A11 epitopes, no response was observed against A1 epitopes.
- Vaccinee 202T7 (HLA A2, B27, C25) made the strongest response to an epitope at positions 131-140 of Gag. The response was highly cross-reactive with D clade Gag expressed from vaccinia, less so with C, and only minimally cross-reactive with A and CRF01.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* p17/p24 Gag
Species (MHC) mouse (H-2^b, H-2^d, H-2^k)
References Iroegbu *et al.* 2000

- The p24 sequence is more conserved than is p17 within patient, and nonsynonymous substitutions are spread evenly throughout its coding regions, not concentrated in CTL epitopes.
- Minor changes in p24 did not alter the immunogenicity in H-2b,d, or k mice, while changes in p17 (92% similarity) did alter immunogenicity.

HXB2 Location Gag
Author Location Gag (SF2)
Epitope
Immunogen Vaccine
Vector/Type: DNA, vaccinia *Strain:* B clade SF2 *HIV component:* Gag, Pol
Species (MHC) mouse (H-2^{bxd})
References Otten *et al.* 2000

- CB6F1 were primed with gag DNA by im injection and challenged with vaccinia expressing Gag/Pol (rVVgag-pol)
- Gag-specific CTL responses were detected by IFNgamma secretion in the spleen, independent of the route (intraperitoneal, intranasal or intrarectal) of rVV gag-pol challenge.
- The gag DNA vaccine induced CTL responses in 4/4 monkeys 2 weeks post immunization, but antibody responses were detected in only 1/4 monkeys after 3 immunizations.
- CTL cross-reactivity against Gag sequences 1-80, 254-323, and 421-496 was observed, suggesting multiple CTL epitope recognition.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Gag
Species (MHC) mouse (H-2^d)
References Qiu *et al.* 2000

- Mice were injected with plasmid DNA at 0, 2 and 4 weeks and lymphocyte proliferation was measured after 6 weeks with recombinant p24 protein.
- Secreted HIV-1 Gag expression vectors generated a stronger response than standard Gag or cytoplasmic Gag expression vectors.
- IFN-gamma levels were increased compared to an undetectable IL-4 response.
- CTL levels were also increased in secreted Gag expression vaccination studies.

HXB2 Location Gag
Author Location Gag (SF2)
Epitope
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade SF2 *HIV component:* Gag, Protease
Species (MHC) macaque, mouse (H-2^d)
References zur Megede *et al.* 2000

- Sequence-modified Rev-independent gag and gag-protease gene constructs lead to increased expression levels and elevated CTL and antibody immunogenicity in BALB/c and CB6F1 mice.
- A CTL response in mice could be detected after a single immunization with codon-optimized gag, using 2 ng of plasmid; wild type gag required 200 ng to detect a response.
- Recognition of 3 different Gag peptide pools was observed, indicating a polyclonal CTL response.
- Significant gag-specific CTL responses were detected in 4/4 rhesus monkeys, in contrast to 1/4 using wildtype gag.

HXB2 Location Gag
Author Location p24
Epitope

Immunogen Vaccine
Vector/Type: coxsackievirus *HIV component:* p24 Gag
Species (MHC) mouse (H-2^d)
References Halim *et al.* 2000

- An avirulent recombinant coxsackievirus (CB4-P) construct was generated that can express p24 Gag sequences – CB4-P is attenuated even in immunodeficient mice and T help responses can be elicited from peptides embedded in a surface loop of the VP1 capsid.
- This paper describes the vaccine strategy and generation of constructs, and employs amino-terminal fusion of Gag sequences to the viral polyprotein with subsequent cleavage to elicit CTL responses via MHC class I presentation in BALB/c mice.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade HXB2, B clade NL43 *HIV component:* Gag, Pol
Species (MHC) mouse (H-2^d)
References Huang *et al.* 2001

- Different HIV strains were used for different regions: gag HXB2, pol NL43
- Mice were immunized with four humanized DNA constructs: GagPol, that would form a pseudoparticle carrying Gag and Pol, Gag, Pol or a GagPol fusion construct.
- The GagPol pseudoparticle, Gag and GagPol fusion construct all elicited strong anti-Gag CTL, but only the GagPol fusion construct elicited strong anti-Pol CTL.

HXB2 Location Gag
Author Location Gag (HXB)
Epitope
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2^d, H-2^b)
Keywords Th1
References Mata *et al.* 2001

- BALB/c and C57BL/6 mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.
- CD4+ Th1 T-cells mediated the Gag specific immunological protection in mice immunized with Lm-Gag and challenged with vaccinia-Gag.
- Gag-specific CTL may enhance viral clearance via IFN-gamma secretion, but are not essential for immunity.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2^d, H-2^b)
Keywords review, Th1
References Mata & Paterson 2000

- BALB/c and C57BL/6 mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.
- This article is a review of L. monocytogenes biology and its potential as a vaccine vector for HIV, comparing to other vector systems, and discussing CD4+ Th1 T-cells mediated Gag specific immunological protection in mice and the Gag CTL response.

II-B-7 Gag/Pol CTL, CD8+, epitopes

HXB2 Location Gag/Pol
Author Location Gag/Pol (ARV-2 SF2)
Epitope
Immunogen Vaccine
Vector/Type: fowlpoxvirus *Strain:* B clade ARV-2, B clade SF2 *HIV component:* Gag, Pol *Adjuvant:* IFNγ
Species (MHC) macaque
References Kent *et al.* 2000

- Vaccination with FPV Gag/Pol-IFN-gamma increased HIV-1 specific CTL and T cell proliferative responses to Gag/Pol antigens, respectively, in infected Macaca nemestrina.
- HIV-1 viral loads remained low and unchanged following vaccinations.

HXB2 Location Gag/Pol
Author Location RT
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12
Species (MHC) mouse
References Kim *et al.* 1997d

- A Gag/Pol or Env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules CD86, gave a dramatic increase in both the cytotoxic and proliferative responses in mice.
- When CD86 was present, CTL response could be detected even without *in vitro* stimulation.

HXB2 Location Gag/Pol
Author Location RT
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords TCR usage
References Gamberg *et al.* 1999

- 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL *in vitro*, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens.
- Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR Vβ gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases.

HXB2 Location Gag/Pol
Author Location
Epitope
Immunogen Vaccine
Vector/Type: adenovirus *HIV component:* Gag-Pol, Nef, Vpr
Species (MHC) mouse
References Muthumani *et al.* 2002

- Vpr can cause cells to go into G2 arrest, and it surpresses immune cell activation and inflammatory cytokine production, so co-immunization of BALB/c mice with recombinant adenovirus expressing Vpr and HIV-1 antigens Nef or Gag/Pol was tested to see if Vpr reduced the immune response to the other HIV antigens.
- Vpr compromised CD8+ T-cell lytic responses and T-helper proliferative responses in mice co-immunized with Vpr and Nef or Gag/Pol.
- In vitro, Vpr reduced T-cell cytokine production of IL-12 and TNFalpha, indicative of Vpr-mediated immune suppression.

II-B-8 Protease CTL, CD8+, epitopes

HXB2 Location Protease (3–11)
Author Location RT (71–79 subtype A, B, D)
Epitope ITLWQRPLV
Subtype A, B, D
Immunogen
Species (MHC) human (A*6802)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*6802 epitope.

HXB2 Location Protease (3–11)
Author Location Pol
Epitope ITLWQRPLV
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human (A*6802)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location Protease (3–11)
Author Location Protease (71–79 LAI)
Epitope ITLWQRPLV
Subtype B
Immunogen
Species (MHC) human (A*6802, A*7401, A19)
Keywords inter-clade comparisons
References Dong 1998

- Predicted on binding motif, no truncations analyzed.
- Clade A/B/D consensus, S. Rowland-Jones, pers. comm.

HXB2 Location Protease (3–11)
Author Location RT (71–79 subtype A, B, D)
Epitope ITLWQRPLV
Subtype A, B, D
Immunogen
Species (MHC) human (A*7401)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*7401 epitope.

HXB2 Location Protease (3–11)
Author Location Pol (59–)
Epitope ITLWQRPLV
Epitope name Pol59
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Protease *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) transgenic mouse (A2)
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.

- This peptide was an intermediate A2 binder, and induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.

HXB2 Location Protease (3–11)
Author Location Pol (59–65)
Epitope ITLWQRPLV
Immunogen HIV-1 infection
Species (MHC) human (A28)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Protease (3–11)
Author Location RT (71–79 LAI)
Epitope ITLWQRPLV
Epitope name P2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A28 supertype)
Keywords HAART, ART, supertype
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location Protease (3–11)
Author Location Pol
Epitope ITLWQRPLV
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A74)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ITLWQRPLV cross-reacts with clades A, B and D.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location Protease (4–14)
Author Location Pol (60–70 SF2)
Epitope TLWQRPLVTIR
Subtype B
Immunogen HIV-1 infection, computer prediction
Species (MHC) human (A*3303)
Assay type Chromium-release assay
Keywords binding affinity, computational epitope prediction
References Hossain *et al.* 2003

- HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing.
- This epitope is one of the 4 that are properly processed.

HXB2 Location Protease (11–20)
Author Location Pol
Epitope VTIKIGGQLK
Epitope name Pol 98
Subtype M
Immunogen Vaccine, in vitro stimulation or selection, computer prediction
Vector/Type: DNA, peptide *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, mouse, humanized mouse (A*1101)
Assay type cytokine production, T-cell Elispot
Keywords inter-clade comparisons, computational epitope prediction, escape, TCR usage, variant cross-recognition or cross-neutralization
References McKinney *et al.* 2004

- This study examined variant recognition of epitopes presented by A*0201 and A*1101. Numerous amino acid substitutions can be introduced into epitopes without disrupting their recognition by CTLs, although epitopes with multiple substitutions were less recognized. An algorithm was constructed for prediction of epitopes capable of inducing responses to a great number of variant epitopes.
- A total of 30 variant forms of Pol 98 were identified. 50% of the variant epitopes were recognized by CTLs from mice immunized with the parental form.
- Pol 98 epitope was present in 71% of HIV sequences of many M group subtypes.

HXB2 Location Protease (11–20)
Author Location Pol (91–100)
Epitope VTILIGGQLK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location Protease (12–20)

Author Location Pol (92–100)
Epitope TIKIGGQLK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location Protease (30–38)
Author Location Pol (subtype B)
Epitope DTVLEEMNL
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A*6802)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi—these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among B and D clade viruses.
- The Clade A version of the epitope: DTVLEDINL.
- This epitope was recognized by two different exposed and uninfected prostitutes.
- This epitope was identified by screening 49 HIV-1 peptides with the predicted A*6802 anchor residue motif x(VT)xxxxxx(VL)

HXB2 Location Protease (30–38)
Author Location Pol (subtype A)
Epitope DTVLEDINL
Subtype A
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A*6802)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 IFNγ responses in the cervix—systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location Protease (30–38)
Author Location RT (85–93 subtype D)
Epitope DTVLEEWNL
Subtype D
Immunogen
Species (MHC) human (A*6802)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*6802 epitope.

HXB2 Location Protease (30–38)
Author Location Pol (subtype A)
Epitope DTVLEDINL
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (A*6802)
Keywords HIV exposed persistently seronegative (HEPS), escape
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- DTVLEDINL was recognized in 3 of the 6 women (ML857, ML1203, and ML1707), and the response was present in the last available sample prior to seroconversion, 3-7 months.
- In each of the three women, 20/20 sequences of the infecting strain had no substitutions in this epitope, all were DTVLEDINL, so there was no evidence for escape.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 3/22 HEPS sex worker controls, ML851, ML1432, and ML1601.

HXB2 Location Protease (30–38)
Author Location Pol (85–93)
Epitope DTVLEDINL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A*6802)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.

- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-A*6802 women, 11/12 HEPS and 6/11 HIV-1 infected women recognized this epitope likelihood ratio 4.4, p value 0.08, and HEPS women tended to respond to DTVLEDINL, infected women tended to ETAYFILKL.
- The dominant response to this HLA allele was to this epitope in 10 of the 11/12 HEPS cases, but in only 4 of the 6/11 HIV-1 infected women.
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.
- Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLN(M/T)LN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24.
- Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion, and the loss of the pre-seroconversion response was not due to sequence variation within these epitopes.
- Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGV/IRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.
- Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion, and the loss of the pre-seroconversion response was not due to sequence variation within the epitope.
- Subject ML 1830 made no detectable response prior to seroconversion, but responded to A*6802 DTVLEDINL and A*6802 ETAYFILKL post-seroconversion.

HXB2 Location Protease (30–38)
Author Location Pol
Epitope DTVLEDINL
Immunogen HIV-1 infection
Species (MHC) human (A*6802)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002

- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.
- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location Protease (30–38)
Author Location (B consensus)
Epitope DTVLEEMNL
Epitope name DL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A68)
Donor MHC A31, A68, B07, B70, Cw7, Cw1
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location Protease (34–42)
Author Location Protease (34–42)
Epitope EEMNLPGRW
Immunogen
Species (MHC) human (B*44)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Protease (34–42)
Author Location Protease
Epitope EEMNLPGRW
Epitope name EW9
Immunogen HIV-1 infection
Species (MHC) human (B44)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords epitope processing, supervised treatment interruptions (STI), immunodominance
References Rodriguez *et al.* 2004

- Protease and Integrase are shown to be frequently targeted by CD8 T-cell responses (23% and 68% of 56 HIV+ patients, respectively). Repsonses tend to cluster in conserved regions of Integrase, although one high conserved region had no responses. CTL frequencies per unit protein length for Protease and Integrase were similar to other HIV non-structural proteins. Three novel, HLA class I-restricted optimal epitopes were found and characterized with fine mapping.
- The epitope includes residue M36 which is a known accessory mutation site in individuals treated with PIs.

HXB2 Location Protease (45–54)
Author Location Pol (45–54 IIIB)
Epitope KMIGGIGGFI
Epitope name pol45-54
Subtype B

Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB
HIV component: Gag-Pol
Species (MHC) humanized mouse (A*0201)
Assay type Intracellular cytokine staining
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance, variant cross-recognition or cross-neutralization, vaccine antigen design
References Singh & Barry 2004

- When A*0201-C3H/J transgenic mice were immunized with plasmids encoding wild-type gag-pol, codon-optimized (CO) gag-pol, and an expression library vaccine expressing 16 fragments of gag-pol fused with ubiquitin for proteosome targeting (ELI), the ELI vaccine produced up to 10-fold higher CD8 T-cell responses than the other two vaccines. In contrast to the wt and CO vaccines, which tended to augment only immunodominant responses, boosting with the ELI vaccine resulted in many CD8 responses against variant epitopes from different HIV-1 clades, and against drug-resistant variants.
- The drug resistant variant of this epitope, kViVgiggfi, was tested. WT and CO vaccines produced low level CD8+ T-cell responses against the B clade form as well as against drug resistant variant, but the ELI vaccine produced much more intense responses against both the WT and the variant, including after boosting.

HXB2 Location Protease (45–54)
Author Location Pol (125–134)
Epitope `KMIGGIGGFI`
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

HXB2 Location Protease (75–84)
Author Location Protease (75–84 MN)
Epitope `VLVGPTPVNI`
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords binding affinity
References Konya *et al.* 1997

- Peptide predicted to be reactive based on HLA-A*0201 binding motif.
- Peptide could stimulate CTL in PBMC from 5/6 seronegative donors.
- Peptide located in a highly conserved region of protease.
- Both 9-mer and 10-mer could stimulate CTL: VLVGPTPVNI and LVGPTPVNI.
- Binding affinity to A*0201 was measured, $C_{1/2\ max}\mu M = 6$ for 10-mer, 3 for 9-mer.
- MAL variant of Pr(75-84 MN), with substitutions V77, G78, and P79, gave reduced binding and CTL recognition.

HXB2 Location Protease (75–84)
Author Location Protease (175–184 MN)
Epitope `VLVGPTPVNI`
Subtype B
Immunogen Vaccine
Vector/Type: DNA, polyepitope *Strain:* B clade MN *HIV component:* gp120, Protease, RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) humanized mouse (A*0201)
Assay type CD8 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance, immunotherapy
References Isaguliants *et al.* 2004

- Immunization of HLA-A*0201-transgenic mice with synthetic genes encoding clusters of human A*0201 CTL epitopes located at the sites of drug resistance mutations, induced RT-specific cellular responses indicating the immunogenicity of these constructs. This vaccine strategy may be a first step towards a therapeutic vaccine against drug-resistant strains.
- This was one of five HLA-A*0201 epitopes from the RT or protease proteins that was included in the polyepitope vaccine. When the transgenic HLA A*0202 mice were vaccinated with the polyepitope construct or with a mixture of RT peptides, a sustained low level CD8+ T-cell gamma IFN response was observed, in contrast to when an intact RT gene was used for vaccination.

HXB2 Location Protease (75–84)
Author Location Pol (75–84 IIIB)
Epitope `VLVGPTPVNI`
Epitope name pol75-84
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB
HIV component: Gag-Pol
Species (MHC) humanized mouse (A*0201)
Assay type Intracellular cytokine staining
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance, variant cross-recognition or cross-neutralization, vaccine antigen design
References Singh & Barry 2004

- When A*0201-C3H/J transgenic mice were immunized with plasmids encoding wild-type gag-pol, codon-optimized (CO) gag-pol, and an expression library vaccine expressing 16 fragments of gag-pol fused with ubiquitin for proteosome targeting (ELI), the ELI vaccine produced up to 10-fold higher CD8 T-cell responses than the other two vaccines. In contrast to the wt and CO vaccines, which tended to augment only immunodominant responses, boosting with the ELI vaccine resulted in

many CD8 responses against variant epitopes from different HIV-1 clades, and against drug-resistant variants.
- The drug resistant variant of this epitope,vlvgptpTnV, was tested. WT and CO vaccines produced low level CD8+ T-cell responses against the B clade form as well as against drug resistant variant, but the ELI vaccine produced much more intense responses against both the WT and the variant, including after boosting.

HXB2 Location Protease (76–84)
Author Location Pol (163–)
Epitope LVGPTPVNI
Epitope name Pol-163
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- LVGPTPVNI binds to 4/5 HLA-A2 supertype alleles: A*0201, A*0202, A*0206 (highest affinity) and A*6802, but not A*0203.
- 1/22 individuals with chronic HIV-1 infection recognized this epitope by ELISPOT.
- 0/12 acutely infected individuals recognized this epitope.

HXB2 Location Protease (76–84)
Author Location Protease (76–84 HXB2)
Epitope LVGPTPVNI
Epitope name PR82V
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Intracellular cytokine staining, Chromium-release assay
Keywords HAART, ART, escape
References Karlsson *et al.* 2003

- This epitope contains two positions that are commonly associated with protease inhibitor escape, lvgptpAni (V82A) and lvgptpvnV (I84V). 29 HIV-1 infected patients (15 were HLA-A2+) with a history of protease inhibitor failure were screened for mutations within the protease gene and CD8+ T cells recognition of the wt and V82A variant peptides. CTL pressure alone, despite high functional avidity, did not drive the V82A substitution. Suprisingly V82A was found more frequently among HLA-A2- individuals (10/14) than HLA-A2+ (7/15), despite the mutation conferring not only drug resistance but CTL escape.
- 8/15 HLA-A2+ patients carried had a Val at position 82; 7/8 of these recognized the WT peptide, but only 3/8 could also recognize V82A.
- 7/15 had the V82A substitution; 2/7 recognized the wt and the V82A mutation, 1/7 recognized only the peptide with the V82A substitution.

HXB2 Location Protease (76–84)
Author Location Protease (76–84)
Epitope LVGPTPVNI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Canada.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords HAART, ART, escape, immunotherapy, variant cross-recognition or cross-neutralization
References Mason *et al.* 2004

- Accumulation of specific antiretroviral drug-resistance mutations in Pol gene was shown to sustain and even enhance the antigenicity and immunogenicity of HIV-1 CTL epitopes in this region. Several different patterns of cross-reactivity and selective recognition of wild-type and variant epitopes were found.
- LVGPTPVNv variant is detected due to appearence of I84V resistance mutation. Three patients receiving PIs had viral sequences obtained, and two had the I84V mutation. EliSpot reactivity to this epitope in either form was evident in these patients, showing drug resistnace can persist coincident with an active CTL response.

HXB2 Location Protease (76–84)
Author Location Pol (156–164)
Epitope LVGPTPVNI
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

II-B-9 Protease-RT CTL, CD8+, epitopes

HXB2 Location Protease-RT (95–5)
Author Location Gag (175–184)
Epitope CTLNFPISPI
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)

Keywords supertype, rate of progression
References Propato *et al.* 2001

- The epitope starts in Protease and ends in RT.
- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)

HXB2 Location Protease-RT (96–5)
Author Location Pol (176–184)
Epitope TLNFPISPI
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

II-B-10 RT CTL, CD8+, epitopes

HXB2 Location RT (3–12)
Author Location RT (LAI)
Epitope SPIETVPVKL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2, B61)
References van der Burg *et al.* 1997

- Recognized by CTL from a long-term survivor, EILKEPVGHGV was also recognized.
- Highly conserved across clades.

HXB2 Location RT (3–12)
Author Location Pol
Epitope SPIETVPVKL
Immunogen
Species (MHC) human (B7)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay.
- SPIETVPVKL was newly identified as HLA-B7 epitope in this study, it had been previously shown to be presented by HLA-A2 and B61.

HXB2 Location RT (3–12)
Author Location Pol
Epitope SPIETVPVKL
Epitope name 1307
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7, A2, B8, B61)
Donor MHC A03, A24, B07, B38, Cw07, Cw12/13; A29, A30, B08, B44, Cw07, Cw16
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for SPIETVPVKL: 12%. Promiscuous epitope binding to A02, B07, B08 and B61.

HXB2 Location RT (5–12)
Author Location RT (5–12)
Epitope IETVPVKL
Immunogen HIV-1 infection
Species (MHC) human (B*4001)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location RT (5–29)
Author Location RT (160–184 HXB2)
Epitope IETVPVKLKPGMDGPKVKQWPLTEE
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Walker *et al.* 1989

- One of five epitopes defined for RT-specific CTL clones in this study.

HXB2 Location RT (14–23)
Author Location Pol
Epitope PGMDGPKVKQ
Epitope name 1276
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A11)

Donor MHC A11, A68, B42, B45, Cw16, Cw17
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for PGMDGPKVKQ:52% Promiscuous epitope binding to A11 or A68, previously published B8.

HXB2 Location RT (18–26)
Author Location RT (185–193 LAI)
Epitope GPKVKQWPL
Subtype B
Immunogen
Species (MHC) human (B*0801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0801 epitope.

HXB2 Location RT (18–26)
Author Location RT (18–26)
Epitope GPKVKQWPL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Meier *et al.* 1995; Menendez-Arias *et al.* 1998

- HIV proteins with mutations in this epitope allowed transactive inhibition of specific CTL-mediated lysis.
- Article reviewed in Menendez-Arias *et al.* [1998], with a discussion of antagonism.

HXB2 Location RT (18–26)
Author Location RT (173–181)
Epitope GPKVKQWPL
Immunogen
Species (MHC) human (B8)
References Goulder *et al.* 1997g; Menendez-Arias *et al.* 1998

- Included in a study of the B8 binding motif.
- Article reviewed in Menendez-Arias *et al.* [1998], with a discussion of antagonism.

HXB2 Location RT (18–26)
Author Location RT (185–193 LAI)
Epitope GPKVKQWPL
Subtype B
Immunogen
Species (MHC) human (B8)
References Sutton *et al.* 1993

- Predicted epitope based on B8-binding motifs, from larger peptide IETVPVKLKPGMDGPKVKQWPLTEE.

HXB2 Location RT (18–26)
Author Location RT (185–193 LAI)
Epitope GPKVKQWPL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Klenerman *et al.* 1995; Menendez-Arias *et al.* 1998

- Naturally occurring antagonist GPRVKQWPL found in viral PBMC DNA and RNA.
- Article reviewed in Menendez-Arias *et al.* [1998] with a discussion of antagonism.

HXB2 Location RT (18–26)
Author Location RT (18–26)
Epitope GPKVKQWPL
Immunogen in vitro stimulation or selection
Species (MHC) human (B8)
Keywords dendritic cells
References Zarling *et al.* 1999

- This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses.
- Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA.
- A weak response to KLTPLCVSL was stimulated using macrophages as the APC.
- No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.

HXB2 Location RT (18–26)
Author Location RT (185–193)
Epitope GPKVKQWPL
Epitope name GPK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, escape, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- Two of the 7/8 study subjects that were HLA B8+ recognized this epitope.
- Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responsiveness against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII peptides – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones.

- Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640 had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy.

HXB2 Location RT (18–26)
Author Location Pol
Epitope GPKVKQWPL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART
References Seth *et al.* 2001

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.

HXB2 Location RT (18–26)
Author Location RT (185–193 SF2)
Epitope GPKVKQWPL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/3 group 2, and 2/2 group 3.

HXB2 Location RT (18–26)
Author Location Pol (171–180)
Epitope GPKVKQWPL
Subtype A, B, C, D
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B8)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- GPKVKQWPL is cross-reactive for clades A, B, C, and D.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location RT (18–26)
Author Location RT (18–26)
Epitope GPKVKQWPL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Day *et al.* 2001

- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.

HXB2 Location RT (18–26)
Author Location RT
Epitope GPKVKQWPL
Epitope name GPK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location RT (18–26)
Author Location Pol (171–180)
Epitope GPKVKQWPL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- One of the patients responded to this peptide with GzB producing cells, while two different patients responded with IFN-gamma producing cells.

HXB2 Location RT (18–26)
Author Location (B consensus)
Epitope GPKVKQWPL
Epitope name GL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A25, A32, B08, B14, Cw7, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location RT (18–27)
Author Location Pol
Epitope GPKVKQWPLT
Immunogen
Species (MHC) human (B7, B8)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay.
- GPKVKQWPLT was confirmed as a previously identified HLA-B8 epitope, and newly identified as an HLA-B7 epitope in this study.

HXB2 Location RT (18–27)
Author Location Pol
Epitope GPKVKQWPLT
Epitope name 1293
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7, B8)
Donor MHC A03, A24, B07, B38, Cw07, Cw12/13; A29, A30, B08, B44, Cw07, Cw16
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for GPKVKQWPLT: 27% Promiscuous epitope binding to B07 and B08.

HXB2 Location RT (33–41)
Author Location RT (33–41 LAI)
Epitope ALVEICTEM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0201 epitope.

HXB2 Location RT (33–41)
Author Location RT (33–41 LAI)
Epitope ALVEICTEL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity, computational epitope prediction
References Samri *et al.* 2000

- This epitope contains the mutation M41L, a mutation induced by nucleosidee reverse transcriptase inhibitors.
- Patient 201#5, (A*0201), was found by ELISPOT to recognize the mutated peptide after zidovudine treatment, but not the wild-type peptide – the mutation M41L gave an increased A2 binding score (http://bimas.dcrt.nih.gov/molbio/hla_bind) compared to the wildtype RT sequence.
- Three additional A*0201 individuals and one B27 individual did not respond to this epitope before or after treatment.
- M41L occurred at anchor positions p2 and p9 in several computer predicted RT epitopes (33-41, 32-41, and 40-49) (http//bimas.dcrt.nih.gov/molbio/hla_bind), and increased the predicted binding affinity for 6 HLA molecules (B2705, B5102, C3, A0201, B2705 and B3901)

HXB2 Location RT (33–41)
Author Location RT (33–41 MN)
Epitope ALVEICTEM
Subtype B
Immunogen Vaccine
Vector/Type: DNA, polyepitope *Strain:* B clade MN *HIV component:* gp120, Protease, RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) humanized mouse (A*0201)
Assay type CD8 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance, immunotherapy
References Isaguliants *et al.* 2004

- Immunization of HLA-A*0201-transgenic mice with synthetic genes encoding clusters of human A*0201 CTL epitopes located at the sites of drug resistance mutations, induced RT-specific cellular responses indicating the immunogenicity of these constructs. This vaccine strategy may be a first step towards a therapeutic vaccine against drug-resistant strains.
- This was one of five HLA-A*0201 epitopes from the RT or protease proteins that was included in the polyepitope vaccine. When the transgenic HLA A*0202 mice were vaccinated with the polyepitope construct or with a mixture of RT peptides, a sustained low level CD8+ T-cell gamma IFN response was observed, in contrast to when an intact RT gene was used for vaccination.

HXB2 Location RT (33–41)
Author Location Pol (132–140 IIIB)
Epitope ALVEICTEM
Epitope name pol132-140
Subtype B
Immunogen Vaccine

Vector/Type: DNA *Strain:* B clade IIIB
HIV component: Gag-Pol
Species (MHC) humanized mouse (A*0201)
Assay type Intracellular cytokine staining
Keywords inter-clade comparisons, vaccine-specific epitope characteristics, immunodominance, variant cross-recognition or cross-neutralization, vaccine antigen design
References Singh & Barry 2004

- When A*0201-C3H/J transgenic mice were immunized with plasmids encoding wild-type gag-pol, codon-optimized (CO) gag-pol, and an expression library vaccine expressing 16 fragments of gag-pol fused with ubiquitin for proteosome targeting (ELI), the ELI vaccine produced up to 10-fold higher CD8 T-cell responses than the other two vaccines. In contrast to the wt and CO vaccines, which tended to augment only immunodominant responses, boosting with the ELI vaccine resulted in many CD8 responses against variant epitopes from different HIV-1 clades, and against drug-resistant variants.
- Different variants of this epitope from different clades were tested. WT and CO vaccines produced low level CD8+ T-cell responses against the B clade form as well as against variants from other clades, but the ELI vaccine produced much more intense responses against the B clade and all variants tested, including after boosting. The variants were: clade A, alTDictem; clade C, atTAicEem; and clade D, alIeicSem.

HXB2 Location RT (33–41)
Author Location RT (33–41)
Epitope ALVEICTEM
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules.

HXB2 Location RT (33–41)
Author Location RT (33–41)
Epitope ALVEICTEM
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- SLYNTVATL was the dominant A2 epitope recognized in patients with chronic infection, except for Subject 11841 who recognized 5/8 epitopes and who had a dominant A-2 response to ALVEICTEM.

HXB2 Location RT (33–41)
Author Location RT (33–41)
Epitope ALVEICTEM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2, A3)
Country Canada.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords HAART, ART, immunotherapy, variant cross-recognition or cross-neutralization
References Mason *et al.* 2004

- Accumulation of specific antiretroviral drug-resistance mutations in Pol gene was shown to sustain and even enhance the antigenicity and immunogenicity of HIV-1 CTL epitopes in this region. Several different patterns of cross-reactivity and selective recognition of wild-type and variant epitopes were found.
- ALVEICTEl variant is detected due to appearence of M41L resistance mutation. The M41L variant peptide was almost always preferentially recognized by CTLs from patients undergoing antiretroviral therapy.

HXB2 Location RT (33–43)
Author Location RT (33–43)
Epitope ALVEICTEMEK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules.
- C. Brander notes that this is an A*0301 epitope in the 1999 database, G. Haas, pers. comm.

HXB2 Location RT (33–43)
Author Location RT (33–43)
Epitope ALVEICTEMEK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0301 epitope.

HXB2 Location RT (33–43)
Author Location RT (33–43)
Epitope ALVEICTEMEK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)

- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.

HXB2 Location RT (33–43)
Author Location RT Pol (188–198)
Epitope ALVICTEMEK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong T-helper cell responses. Only patients starting with moderately high viral load (VL) were able to reduce the VL set point. HIV-1 specific CD8+ T-cell responses were shown to increase significantely until the end of the follow up.
- Less than 2 of 14 patients recognized this epitope.

HXB2 Location RT (38–52)
Author Location RT (203–209)
Epitope CTEMEKEGKISKIGP
Immunogen Vaccine
Vector/Type: Salmonella *HIV component:* RT
Species (MHC) mouse (H-2^{d})
References Burnett *et al.* 2000

- A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV epitope in the Lpp-OmpA-HIV fusion protein, induced a specific CTL response in BALB/c mice (<15% lysis assayed by Cr-release of target cells)

HXB2 Location RT (38–52)
Author Location RT (205–219 BRU)
Epitope CTEMEKEGKISKIGP
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* RT
Species (MHC) mouse (H-2^{k})
Keywords review
References De Groot *et al.* 1991; Menendez-Arias *et al.* 1998

- Murine and human helper and CTL epitope.
- Epitope noted in a review by Menendez-Arias *et al.* [1998] to be located in the "fingers" domain of RT and is a helper and CTL epitope.

HXB2 Location RT (38–52)
Author Location RT (205–219)
Epitope CTEMEKEGKISKIGP
Immunogen HIV-1 infection
Species (MHC) human (broad)
Keywords review
References Hosmalin *et al.* 1990; Menendez-Arias *et al.* 1998

- Murine and human helper and CTL epitope.
- Epitope noted in a review by Menendez-Arias *et al.* [1998] to be located in the "fingers" domain of RT and is a helper and CTL epitope.

HXB2 Location RT (39–47)
Author Location RT (206–214)
Epitope TEMEAEGKI
Immunogen in vitro stimulation or selection
Species (MHC) mouse
Keywords TCR usage
References Leggatt *et al.* 1997

- Ala-substituted nonamer-peptide used to test a non-radioactive assay for murine CTL recognition of peptide-MHC class I complexes.
- The new assay is CTL adherence assay (CAA), and is based on the discovery that CTL develop adhesive properties upon TCR triggering.
- Substitutions in TEMEAEGKI that reduce cytolytic activity were correctly detected by CAA.

HXB2 Location RT (39–47)
Author Location RT
Epitope TEMEKEGKI
Immunogen
Species (MHC) mouse (H-2K^{k})
References Leggatt *et al.* 1998

- Epitope variants were examined for CTL response in concert with H-2K^{k} MHC class I binding – all of the following combinations were observed: (i) two single mutations which did not alone abrogated CTL activity did abrogate activity when combined, (ii) loss of recognition of a single substitution could be restored by an additional substitution, and (iii) sometimes there was recognition of two single substitutions as well as the combination of those substitutions.
- 2E and 9I are anchor residues for H-2K^{k} – if you have M in the third position, it enhances H-2K^{k} binding 10-fold, but polymorphism at this site is important for the overall conformation of the peptide and can influence T cell recognition.

HXB2 Location RT (42–50)
Author Location RT (42–50 LAI)
Epitope EKEGKISKI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5101 epitope.

HXB2 Location RT (42–50)
Author Location RT (42–50 LAI)
Epitope EKEGKISKI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B51)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules.

HXB2 Location RT (42–50)
Author Location RT (42–50)
Epitope EKEGKISKI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location RT (57–65)
Author Location Pol (236–244)
Epitope NTPVFAIKK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location RT (57–66)
Author Location Pol
Epitope NTPVFAIKKK
Epitope name 1274
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) chimpanzee, goat, baboon (A11, A68, B8)
Donor MHC A01, A68, B15, B40, Cw03; A25, A68, B18, B27
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, supertype, computational epitope prediction, immunodominance, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for NTPVFAIKKK:53%. Epitope binds to A11 and A68 supertype, and is immunodominant.

HXB2 Location RT (73–82)
Author Location RT (73–82)
Epitope KLVDFRELNK
Immunogen HIV-1 infection
Species (MHC) human (A*03)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location RT (73–82)
Author Location RT (73–82 LAI)
Epitope KLVDFRELNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Samri *et al.* 2000

- This epitope contains the mutation L74V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors.
- The wild-type, but not the mutated peptide, was recognized before and after zidovudine treatment in A3-restricted patients 252#0 and 252#4.
- Mutation L74V affects the p2 anchor position in RT epitopes and was predicted to reduce binding to A3 (http://bimas.dcrt.nih.gov/molbio/hla_bind)

HXB2 Location RT (73–82)
Author Location RT (228–237)
Epitope KLVDFRELNK
Epitope name A3-KK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.

- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 3/7 individuals began to have detectable responses to this epitope after STI.

HXB2 Location RT (73–82)
Author Location RT (73–82)
Epitope KLVDFRELNK
Epitope name A3-KK10 Pol
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response, but in this case the epitope did not vary.

HXB2 Location RT (73–82)
Author Location Pol
Epitope KLVDFRELNK
Epitope name 1340
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A23, B49, B57, C?; A02, A03, B08, B51, Cw01, Cw07; A03, A11, B14, B05, Cw08
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for KLVDFRELNK: 36%.

HXB2 Location RT (73–82)
Author Location (B consensus)
Epitope KLVDFRELNK
Epitope name KK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, B07, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location RT (93–101)
Author Location (LAI)
Epitope GIPHPAGLK
Subtype B
Immunogen
Species (MHC) (A3)
Keywords optimal epitope
References Altfeld 2000; Frahm *et al.* 2004

HXB2 Location RT (93–101)
Author Location RT (248–257)
Epitope GIPHPAGLK
Epitope name A3-GK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.

HXB2 Location RT (93–101)
Author Location RT (93–101)
Epitope GIPHPAGLK
Epitope name A3-GK9 Pol
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ

Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response, but in this case the epitope did not vary.

HXB2 Location RT (93–101)
Author Location Pol
Epitope GIPHPAGLK
Epitope name 1337
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A23, B49, B57, C?
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for GIPHPAGLK: 20%.

HXB2 Location RT (93–101)
Author Location (B consensus)
Epitope GIPHPAGLK
Epitope name GK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, B07, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location RT (93–102)
Author Location Pol (240–249 93TH253 subtype CRF01)
Epitope GIPHPAGLKK
Epitope name P248-257
Subtype CRF01_AE
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11 and after a second stimulation *in vitro* gave a strong response in HEPS study subject 128 who was HLA A11/A33.

HXB2 Location RT (93–102)
Author Location Pol (240–249 93TH253 subtype CRF01)
Epitope GIPHPAGLKK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it.
- This epitope was highly conserved in other subtypes, and exact matches were common.

HXB2 Location RT (98–113)
Author Location Pol (254–264 BH10, LAI)
Epitope AGLKKKKSVTVLDVGD
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is GLKKKKSVTVL) has similarity with the CD166 antigen (activated leukocyte-cell adhesion molecule), fragment GLKKRESLTLI.

HXB2 Location RT (98–113)
Author Location RT (252–266)
Epitope AGLKKKKSVTVLDVGD
Immunogen HIV-1 infection

Species (MHC) human (Cw4)
References Bernard *et al.* 1998

- This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population.
- No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs.

HXB2 Location RT (103–117)
Author Location RT (257–251)
Epitope KKSVTVLDVGDAYFS
Immunogen HIV-1 infection
Species (MHC) human (Cw4)
References Bernard *et al.* 1998

- This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune.
- No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs.

HXB2 Location RT (107–115)
Author Location RT (262–270 IIIB)
Epitope TVLDVGDAY
Immunogen
Species (MHC) (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*3501 epitope.

HXB2 Location RT (107–115)
Author Location RT (262–270 IIIB)
Epitope TVLDVGDAY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords review, responses in children, mother-to-infant transmission
References Menendez-Arias *et al.* 1998; Wilson *et al.* 1996

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.
- TVLDMGDAC is a naturally occurring variant that is less reactive.
- Menendez-Arias *et al.* [1998], in a review, notes that this epitope includes a catalytic residue (Asp-110) in the active site of RT.

HXB2 Location RT (107–115)
Author Location Pol (262–270 IIIB)
Epitope TVLDVGDAY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- An additional variant that gave a positive CTL response: TVLDMGDAC.

HXB2 Location RT (107–115)
Author Location Pol (262–270)
Epitope TVLDVGDAY
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location RT (107–115)
Author Location RT (262–270 SF2)
Epitope TVLDVGDAY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3.

HXB2 Location RT (107–115)
Author Location
Epitope TVLDVGDAY
Epitope name Pol-TY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B35, 8/21 (38%) recognized this epitope.

HXB2 Location RT (107–115)
Author Location Pol
Epitope TVLDVGDAY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Donor MHC A3, A11, B35, B51
Keywords mother-to-infant transmission
References Sabbaj *et al.* 2002a

- IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release.
- T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with either of two overlapping peptides that carry known B35 epitope TVLDVGDAY.
- The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.

HXB2 Location RT (107–115)
Author Location RT (107–115)
Epitope TVLDVGDAY
Subtype AG
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Canada.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords HAART, ART, immunotherapy, variant cross-recognition or cross-neutralization
References Mason *et al.* 2004

- Accumulation of specific antiretroviral drug-resistance mutations in Pol gene was shown to sustain and even enhance the antigenicity and immunogenicity of HIV-1 CTL epitopes in this region. Several different patterns of cross-reactivity and selective recognition of wild-type and variant epitopes were found.
- TiLDVGDAY, TVLDVGDAf and TiLDVGDAf variants are detected due to appearence of V108I and Y115F resistance mutations. Complete cross-reactivity of wild-type and variant peptides was observed.

HXB2 Location RT (107–115)
Author Location RT Pol (262–270)
Epitope TVLDVGDIY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/9 patients recognized this epitope.

HXB2 Location RT (108–118)
Author Location RT (267–277)
Epitope VLDVGDAYFSV
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
References van der Burg *et al.* 1996

- High dissociation rate, but immunogenic in primary CTL induction after repeated stimulations with peptide.
- CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual.

HXB2 Location RT (108–118)
Author Location RT (267–277)
Epitope VLDVGDAYFSV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords dendritic cells
References Kundu *et al.* 1998b

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients.
- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated.
- VLDVGDAYFSV is a conserved HLA-A2 epitope included in this study – 4/6 patients had this sequence as their HIV direct sequence, but only one of these had a detectable CTL response – the other two had the sequences EEDVGDAYFSV and ELDVGDAYFSV and no detectable CTL response.

HXB2 Location RT (108–118)
Author Location RT (267–277)
Epitope VLDVGDAYFSV
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
References van der Burg *et al.* 1995

- Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor.
- VLDVGDAYFSV is in a functional domain.

HXB2 Location RT (108–118)
Author Location RT Pol (263–273)
Epitope VLDVGDAYFSV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 19 patients recognized this epitope.

HXB2 Location RT (108–118)

Author Location Pol (263–273)
Epitope VLDVGDAYFSV
Immunogen HIV-1 infection
Species (MHC) human (A2, A*0201)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location RT (108–122)
Author Location RT (257–251)
Epitope VLDVGDAYFSVPLDE
Immunogen HIV-1 infection
Species (MHC) human (Cw4)
References Bernard *et al.* 1998

- This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population.
- No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs.

HXB2 Location RT (113–120)
Author Location Pol (268–275 SF2)
Epitope DAYFSVPL
Immunogen HIV-1 infection
Species (MHC) human (B*5101, B24)
Keywords inter-clade comparisons, rate of progression
References Tomiyama *et al.* 1999

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA -B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed.
- Four of the six epitopes were highly conserved among B subtype sequences, DAYFSVPL is conserved.

HXB2 Location RT (113–120)
Author Location RT (113–120)
Epitope DAYFSVPL
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location RT (116–135)
Author Location Pol (271–290)
Epitope FSVPLDEDFRKYTAFTIPSI
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location RT (117–126)
Author Location Pol (264–273 93TH253 subtype CRF01)
Epitope SVPLDESFRK
Epitope name P272-281
Subtype CRF01_AE
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope after a second stimulation *in vitro* gave a strong response in HEPS study subject 128 who was HLA A11/A33.

HXB2 Location RT (117–126)
Author Location Pol (264–273 93TH253 subtype CRF01)
Epitope SVPLDESFRK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.

- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 3/8 tested FSWs recognized it.
- This epitope was only conserved in CRF01, and subtype A and B, and exact matches were uncommon.

HXB2 Location RT (118–127)
Author Location (C consensus)
Epitope VPLDEDFRKY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*35)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location RT (118–127)
Author Location RT (273–282 SF2)
Epitope VPLDKDFRKY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords review
References Menendez-Arias *et al.* 1998; Tomiyama *et al.* 1997

- A CTL clone responsive to this epitope was obtained.
- 4/7 B35-positive individuals had a CTL response to this epitope.
- A K to E substitution at position 5 abrogates specific lysis, and reduces binding to B*3501.
- Menendez-Arias *et al.* [1998], in a review, notes that a Glu to Lys (E to K) change abrogates CTL activity, but that both VPLDEDFRKY and VPLDKDFRKY can serve as HLA-B35 epitopes, so the change must alter T cell receptor binding – residues in this epitope may be important for polymerase activity.

HXB2 Location RT (118–127)
Author Location RT (273–282 IIIB)
Epitope VPLDEDFRKY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*3501 epitope.

HXB2 Location RT (118–127)
Author Location Pol (273–282)
Epitope VPLDKDFRKY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 2000a

- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A.
- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals.
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm.
- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

HXB2 Location RT (118–127)
Author Location (SF2)
Epitope VPLDEDFRKY
Epitope name HIV-B3501-SF2-4
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 2000b

- B*3501 VPLDEDFRKY tetramer binding did not inhibit CTL activity of a clone that react with both HLA-B*3501 than HLA-B*5101 presentation of the epitope IPLTEEAEL.

HXB2 Location RT (118–127)
Author Location RT (118–127)
Epitope VPLDEDFRKY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Donor MHC A*2301, B*3501, B*1503 (B72), Cw2, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.

- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location RT (118–127)
Author Location RT (273–282 IIIB)
Epitope VPLDEDFRKY
Immunogen HIV-1 infection
Species (MHC) human (B*3501, B35)
References Shiga *et al.* 1996

- Binds HLA-B*3501.

HXB2 Location RT (118–127)
Author Location (SF2)
Epitope VPLDKDFRKY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, rate of progression, escape
References Kawana *et al.* 1999

- HLA B35 is associated with rapid disease progression.
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals.
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation.
- ––E–- was found in 8/10 of the B35+ individuals, and three of the B35- individuals – the D –> E substituted peptide had similar binding affinity to B35 and was equally susceptible to a CTL clone.

HXB2 Location RT (118–127)
Author Location RT (273–282 IIIB)
Epitope VPLDEDFRKY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords inter-clade comparisons
References Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by three lab workers accidentally infected with HIV-1 IIIB.
- VPLDKDFRKY, a variant found in HIV MN, was not recognized.
- VPHDEDFRKY, a variant found in HIV YU2, was not recognized.
- This epitope was type-specific and conserved in only one other B subtype sequence.

HXB2 Location RT (118–127)
Author Location RT (273–282 SF2)
Epitope VPLDEDFRKY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 1/1 group 3.

HXB2 Location RT (118–127)
Author Location
Epitope VPLDEDFRKY
Epitope name Pol-VY10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B35, 5/21 (24%) recognized this epitope.

HXB2 Location RT (118–127)
Author Location RT Pol (273–282)
Epitope VPLDEDFRKY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/9 patients recognized this epitope.

HXB2 Location RT (126–135)
Author Location RT (293–302 HXB)
Epitope KYTAFTIPSI
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART
References Shankar *et al.* 1998

- A novel CTL clone was defined with a panel of recombinant vaccinia-RT-infected B-LCL target cells using PBMCs donated by a patient who was HIV-seropositive for 6 years and had not received any antiretroviral therapy.

- There is evidence that some CTL epitopes are poorly presented on the surface of infected cells, but this RT epitope was recognized as effectively on HIV-infected cells as on peptide-pulsed targets.

HXB2 Location RT (127–135)
Author Location RT (127–135)
Epitope YTAFTIPSV
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location RT (127–135)
Author Location Pol (316–)
Epitope YTAFTIPSI
Epitope name Pol-316
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- 2/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT.
- 0/12 acutely infected individuals recognized this epitope.
- YTAFTIPSI binds to five HLA-A2 supertype alleles: A*0201, A*0202,A*0203, A*0206 and A*6802 (highest affinity)

HXB2 Location RT (127–135)
Author Location Pol (306–314)
Epitope YTAFTIPSI
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)

HXB2 Location RT (128–135)
Author Location
Epitope TAFTIPSI
Epitope name Pol-TI8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0217, B*5101)
Donor MHC A*0201 A*0217 B*0801 B*4002 Cw*0303 Cw*070
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Patient 01RCH46 was Hispanic, on HAART, and had a viral load of 21000 and CD4 count of 623 – she also recognized GELDRWEKI, p17(11-19), HLA B*4002, and KETINEEAA p24(70-78), HLA B*4002.
- Among HIV+ individuals who carried HLA A*02, 7/36 (19%) recognized this epitope, two of which also carried B*5101 which can also restrict this epitope.

HXB2 Location RT (128–135)
Author Location RT (295–302 IIIB)
Epitope TAFTIPSI
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5101 epitope.

HXB2 Location RT (128–135)
Author Location Pol (283–290 SF2)
Epitope TAFTIPSI
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords inter-clade comparisons, rate of progression
References Tomiyama *et al.* 1999

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed.
- Four of the six epitopes were highly conserved among B subtype sequences, but TAFTIPSI is somewhat variable.

HXB2 Location RT (128–135)
Author Location RT (295–302)
Epitope TAFTIPSI

Epitope name P5
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords HAART, ART, escape
References Samri *et al.* 2000

- The epitope TAFTIPSI was recognized by patient 246#1 in a study of the effects of therapy escape mutations on CTL recognition.

HXB2 Location RT (128–135)
Author Location RT (128–135 IIIB)
Epitope TAFTIPSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords epitope processing, escape
References Moore *et al.* 2002b

- HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing.
- TAFTIPSI was one of two epitopes characterized in detail. C-terminal I135x substitutions were associated with people who carried HLA-B5 – 39/40 (98%) of HLA-B*5101 individuals had substitutions in this position, while only 127/431 (29%) who did not have HLA-B*5101 did. The predominant substitution was kytaftipsT, and this mutation is predicted to abrogate binding to HLA-B*5101.

HXB2 Location RT (128–135)
Author Location RT (295–302 IIIB)
Epitope TAFTIPSI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Keywords review
References Menendez-Arias *et al.* 1998; Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.
- TAFTIPST, a variant found in HIV-1 CAM1, was also recognized but 100-fold more peptide was needed.
- TAFTIPSV, a variant found in HIV-1 VE1RT, was also recognized, but 10-fold more peptide was needed.
- TVFTIPSI, a variant found in HIV-1 MANC, was also recognized.
- Menendez-Arias *et al.* [1998], in a review, notes that this epitope includes a region near the active site of RT – the substitution of the position two conservative change from A to V decreases CTL recognition.

HXB2 Location RT (128–135)
Author Location RT (295–302)
Epitope TAFTIPSI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- Three of the four individuals that responded to SLYNTVATL recognized additional HIV epitopes, and all three were also HLA B51 and recognized this epitope as well as other epitopes.

HXB2 Location RT (128–135)
Author Location RT (295–302)
Epitope TAFTIPSI
Epitope name TAF
Immunogen HIV-1 infection
Species (MHC) human (B51)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- None of the 8 study subjects recognized this epitope but none were HLA B51+

HXB2 Location RT (128–135)
Author Location RT (295–302 LAI)
Epitope TAFTIPSI
Epitope name P5
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B51)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location RT (128–135)
Author Location Pol
Epitope TAFTIPSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B51)

Donor MHC A3, A11, B35, B51
Keywords mother-to-infant transmission
References Sabbaj *et al.* 2002a

- IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release.
- T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with either of two overlapping peptides that carry known B51 epitope TAFTIPSI.
- The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.

HXB2 Location RT (128–135)
Author Location RT (128–135)
Epitope TAFTIPSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A*0201, A11, B51, B61, Cw2, Cw14
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location RT (128–135)
Author Location RT (128–135)
Epitope TAFTIPSI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 5 epitopes from this individual that varied over time where the internal mutations became fixed; a dramatic decrease in CTL activity against the wild type epitope was observed as the mutation arose. The taftipsT variant residue found at 47 months postseroconversion.

HXB2 Location RT (130–144)
Author Location RT (130–144)
Epitope FTIPSINNETPGIRY
Immunogen HIV-1 infection
Species (MHC) human (A25)
Assay type Chromium-release assay
Keywords assay standardization/improvement
References Lubong *et al.* 2004

- Using IL7 or IL15 in culturing of HIV-1 specific CTL clones was inferior to using IL-2 alone and the addition of these cytokines to IL-2 did not show any advantage. Neither proliferation, survival or lytic capacity of HIV-1-specific CTLs was significantly enhanced by addition of IL7 or IL15.

HXB2 Location RT (151–159)
Author Location Pol (306–314 SF2)
Epitope QGWKGSPAI
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords inter-clade comparisons, rate of progression
References Tomiyama *et al.* 1999

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS.
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed.
- Four of the six epitopes were highly conserved among B subtype sequences, QGWKGSPAI is conserved.

HXB2 Location RT (151–168)
Author Location RT (151–168 HXB2)
Epitope QGWKGSPAIFQSSMTKIL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started

treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location RT (153–165)
Author Location RT (308–320)
Epitope WKGSPAIFQSSMT
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords responses in children, mother-to-infant transmission
References Brander & Walker 1995
- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.

HXB2 Location RT (153–165)
Author Location Pol (308–320)
Epitope WKGSPAIFQSSMT
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Ferrari *et al.* 2000
- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location RT (153–167)
Author Location RT (SF2)
Epitope WKGSPAIFQSSMTKI
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2001a
- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- RT peptides SQIYPGIKVRQLCKL and WKGSPAIFQSSMTKI were recognized.

HXB2 Location RT (156–164)
Author Location RT (311–319 SF2)
Epitope SPAIFQSSM
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords review
References Menendez-Arias *et al.* 1998; Tomiyama *et al.* 1997
- A CTL clone responsive to this epitope was obtained.
- Only 1/7 B35-positive individuals had a CTL response to this epitope.
- Menendez-Arias *et al.* [1998], in a review, notes that this epitope is near the active site of RT.

HXB2 Location RT (156–164)
Author Location (C consensus)
Epitope SPAIFQSSM
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*8101, B*0702)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004
- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location RT (156–164)
Author Location RT (311–319 SF2)
Epitope SPAIFQSSM
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords review
References Menendez-Arias *et al.* 1998; Shiga *et al.* 1996
- Binds HLA-B*3501.
- Menendez-Arias *et al.* [1998], in a review, notes that this epitope includes catalytic residues in the active site of RT.

HXB2 Location RT (156–164)
Author Location Pol (311–319)
Epitope SPAIFQSSM
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Ferrari *et al.* 2000
- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location RT (156–164)
Author Location RT Pol (311–319)
Epitope SPAIFQSSM
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Spain.

Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/9 patients recognized this epitope.

HXB2 Location RT (156–164)
Author Location Pol (156–164 HXB2)
Epitope SPAIFQSSM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, immunodominance
References Hay *et al.* 1999

- CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201.
- The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted.
- Despite the initial narrow response to two epitopes, no other CTL responses developed.
- No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak.
- Variants of this epitopes were observed *in vivo* (spaifqCsm, spSifqssm), but the binding motifs for B7 were preserved (P2, and C-term aromatic or hydrophobic)

HXB2 Location RT (156–164)
Author Location Pol
Epitope SPAIFQSSM
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Islam *et al.* 2001

- Subject 053i was followed longitudinally from acute infection through death, and had rapid progression to AIDS.
- This individual had a dominant response to IPRRIRQGL with strong *in vivo* activated responses and *in vitro* stimulated memory responses and a subdominant response to SPAIFQSSM – during the course of disease progression (4 Years), the functional CTL responses were lost and no sequence variation occurred with in both epitopes, but CTL clones specific for IPRRIRQGL persisted throughout.

HXB2 Location RT (156–164)
Author Location RT (323–331 SF2)
Epitope SPAIFQSSM
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3.

HXB2 Location RT (156–164)
Author Location RT (156–164)
Epitope SPAIFQSSM
Epitope name B7-SM9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 3/4 individuals had detectable responses to this epitope after STI.

HXB2 Location RT (156–164)
Author Location RT (156–164)
Epitope SPAIFQSSM
Epitope name B7-SM9 Pol
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response; this epitope did not vary.

HXB2 Location RT (156–164)
Author Location
Epitope SPAIFQSSM
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement, epitope processing
References Draenert *et al.* 2004a

- 96% of optimally defined epitopes have one of only nine amino acids serving as the C-terminal anchor position. Seven amino acids are never found in this position and four are only present in 4% of cases. CD8 T-cell response to an epitope is shown to be best detected when the epitope is situated at the C-terminal end of a longer peptide, and authors suggest that Elispot reagents would be better designed if peptides ended on known C-terminal anchors.
- SPAIFQSSM is suggested to be the optimal epitope instead of SPAIFQSSMT.

HXB2 Location RT (156–164)
Author Location (B consensus)
Epitope SPAIFQSSM
Epitope name SM9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, B07, Cw7
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location RT (156–165)
Author Location RT (311–319 LAI)
Epitope SPAIFQSSMT
Epitope name P4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, escape
References Samri *et al.* 2000

- This epitope contains the mutation P157S which can be induced by nucleosidee reverse transcriptase inhibitors.
- It was recognized by patient 252#0 in a study of the effects of therapy escape mutations on CTL recognition.

HXB2 Location RT (156–165)
Author Location RT (311–319 SF2)
Epitope SPAIFQSSMT
Immunogen
Species (MHC) human (B7)
Keywords review
References Brander & Walker 1997; Menendez-Arias *et al.* 1998

- Pers. comm. from C. Hey and D. Ruhl to C. Brander and B. Walker.
- Menendez-Arias *et al.* [1998], in a review, notes that this epitope includes catalytic residues in the active site of RT.

HXB2 Location RT (156–165)
Author Location RT (311–319 SF2)
Epitope SPAIFQSSMT
Epitope name P4
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location RT (156–165)
Author Location Pol
Epitope SPAIFQSSMT
Immunogen
Species (MHC) human (B7)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay.
- SPAIFQSSMT was confirmed as a previously identified HLA-B7 epitope in this study.

HXB2 Location RT (156–165)
Author Location RT (IIIB)
Epitope SPAIFQSSMT
Subtype B

Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords epitope processing, escape
References Moore *et al.* 2002b

- HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing.
- HLA-B7+ individuals with a S162x (18/33) substitution had higher viral loads than those that did not, suggesting escape was associated with diminished immune control of viremia.

HXB2 Location RT (156–165)
Author Location Pol
Epitope SPAIFQSSMT
Epitope name 1306
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, A24, B07, B38, Cw07, Cw12/13
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for SPAIFQSSMT: 13%

HXB2 Location RT (156–165)
Author Location RT Pol (311–319)
Epitope SPAIFQSSMT
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/7 patients recognized this epitope.

HXB2 Location RT (158–166)
Author Location RT (325–333 LAI)
Epitope AIFQSSMTK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0301 epitope.

HXB2 Location RT (158–166)
Author Location
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location RT (158–166)
Author Location Pol
Epitope AIFQSSMTK
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human, macaque (A*0301, A11, A33)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected

to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location RT (158–166)
Author Location RT (325–333 LAI)
Epitope AIFQSSMTK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is an A*1101 epitope.

HXB2 Location RT (158–166)
Author Location Pol (313–321)
Epitope AIFQSSMTK
Subtype B, CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords inter-clade comparisons
References Fukada *et al.* 2002
- Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals.
- AIFQSSMTK is commonly found in viruses representing subtypes A-E. It was strongly recognized by CTL from 2/5 B clade infected Japanese subjects, and 5/6 E clade infected Thai subjects.

HXB2 Location RT (158–166)
Author Location RT (313–321)
Epitope AIFQSSMTK
Subtype B, CRF01_AE
Immunogen
Species (MHC) human (A*1101)
Country Thailand.
Keywords HIV exposed persistently seronegative (HEPS), structure
References Li & Bouvier 2004
- HLA-A*1101 has been associated with resistance to acquisition of HIV-1 infection in female sex-workers in Thailand. Its crystal structure has been determined in association with two immunodominant A*1101 HIV-1 CTL epitopes. Its anchor residues are confirmed as P2(Ile/Val) and C-term (Lys). The backbone conformation of the peptides is defined as two bulges separated by a secondary anchor residue (P6 Ser or Met) that may offer various advantages in the selection and presentation of CTL epitopes by HLA-A*1101.

HXB2 Location RT (158–166)
Author Location RT (325–333)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A*1101, A3, A*0301, A*6801)
References Menendez-Arias *et al.* 1998; Threlkeld *et al.* 1997
- Study of the fine specificity of an A3-like super-type epitope (the A3 super-type includes A*0301, A*1101, A*3101, A*3301, and A*6801)
- A3 super-type is characterized by a hydrophobic or hydroxyl containing anchor residue at position 2, and a positive charge in the C-term position.
- While most lines were specific, promiscuous cloned CTL lines were also derived from HIV+ donors that could recognize epitope presented by either A3 or A11 or A*6801.
- Alanine substitutions throughout the epitope and natural variants indicate that the same amino acid positions are critical for presentation by either MHC molecule, A3 or A11.
- AIFQSSMTK is presented by three members of the A3 superfamily: A*0301, A*1101, and A*6801, and the naturally occurring variants A1S and K9R are recognized with similar efficiency to wild type epitope – AIFQRSMTR can also bind to two additional members of the A3 superfamily, A*3101 and A*3301.

HXB2 Location RT (158–166)
Author Location RT
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Wagner *et al.* 1998a
- CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules.

HXB2 Location RT (158–166)
Author Location RT (325–333 LAI)
Epitope AIFQSSMTK
Subtype B
Immunogen Peptide-HLA interaction
Species (MHC) human (A11)
References Menendez-Arias *et al.* 1998; Zhang *et al.* 1993
- Exploration of A11 binding motif, based on Nixon *et al.* 1991.

HXB2 Location RT (158–166)
Author Location RT (325–333 LAI)
Epitope AIFQSSMTK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords review

References McMichael & Walker 1994
- Review of HIV CTL epitopes.

HXB2 Location RT (158–166)
Author Location Pol (305–313 93TH253 subtype CRF01)
Epitope AIFQSSMTK
Epitope name P313-321
Subtype CRF01_AE
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001
- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33.
- This epitope was strongly reactive in HIV+ study subjects 053 and 184 who carried HLA-A11.

HXB2 Location RT (158–166)
Author Location Pol (305–313 93TH253 subtype CRF01)
Epitope AIFQSSMTK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001
- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined.
- 6/8 tested FSWs recognized this epitope.
- An HLA-A11 tetramer was made for this epitope, which was recognized by two subjects – and both subjects had expanded tetramer staining T-cell populations after *in vitro* stimulation.
- This epitope was highly conserved in other subtypes, and exact matches were common.

HXB2 Location RT (158–166)
Author Location RT (158–166 IIIB)
Epitope AIFQSSMTK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords epitope processing, escape
References Moore *et al.* 2002b
- HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing.
- HLA-A11+ individuals with a K166x (4/19) substitution had higher viral loads than those that did not, suggesting escape was associated with diminished immune control of viremia.

HXB2 Location RT (158–166)
Author Location Pol
Epitope SIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A11)
Donor MHC A2, A11, B8, B60, Bw6
Keywords HAART, ART
References Appay *et al.* 2002
- Four HIV patients with prolonged clinically successful antiviral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

HXB2 Location RT (158–166)
Author Location Pol (325–333)
Epitope AIFQSSMTK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11, A*0301, A33)
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004
- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- One of the patients responded to this peptide with GzB producing cells, while none of the patients responded with IFN-gamma producing cells.

HXB2 Location RT (158–166)
Author Location RT (B consensus)
Epitope AIFQSSMTK
Epitope name ATK9
Immunogen HIV-1 infection
Species (MHC) human (A11, A3)

Donor MHC A02, A11, B18, B44, Cw5, Cw12; A03, B14, B60, Cw3, Cw7; A01, A03, B08, B14, Cw7, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, cross-presentation by different HLA, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 3/9 individuals recognized this epitope, two presented by HLA-A3, one presented by HLA-A11.

HXB2 Location RT (158–166)
Author Location RT (325–333 IIIB)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords responses in children, mother-to-infant transmission
References Wilson *et al.* 1996

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.
- AIFQSSMTR and AILQSSMTK, naturally occurring variants, were found in infant, and are recognized.
- TISQSSMTK, a naturally occurring variant, was found in infant and is not recognized.

HXB2 Location RT (158–166)
Author Location RT (325–333 LAI)
Epitope AIFQSSMTK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords inter-clade comparisons
References Cao *et al.* 1997a

- The consensus peptide of B and D clade viruses is AIFQSSMTK.
- The consensus peptide of a subset of As is AIFQASMTK and it is less able to stimulate the CTL clone.
- The consensus peptide of a subset of As is SIFQSSMTK and is as reactive as the originally defined epitope.

HXB2 Location RT (158–166)
Author Location Pol (325–333 IIIB)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- One variant found in an infant gave a positive CTL response: AIFQSSMTR.
- AIFLSSMTK and TISQSSMTK were escape mutants.

HXB2 Location RT (158–166)
Author Location RT (325–333 SF2)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 0/7 group 1, 0/4 group 2, and 1/2 group 3.

HXB2 Location RT (158–166)
Author Location RT (158–166)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.
- In two of the subjects, AIFQSSMTK was the dominant epitope.

HXB2 Location RT (158–166)
Author Location RT Pol (313–321)
Epitope AIFQSSMTK
Epitope name A3-ATK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)

Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 3/7 individuals began to have detectable responses to this epitope after STI.

HXB2 Location RT (158–166)
Author Location RT (158–166)
Epitope AIFQSSMTK
Epitope name A3-AK9 Pol
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant aifqssmIk. The CTL response to the second variant was zero or low at all timepoints. The CTL response to the first variant was also low, and declined over time.

HXB2 Location RT (158–166)
Author Location RT (158–166)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location RT (158–166)
Author Location RT Pol (313–333)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/14 patients recognized this epitope.

HXB2 Location RT (158–166)
Author Location RT (325–333 LAI)
Epitope AIFQSSMTK
Epitope name P3
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords HAART, ART, supertype
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location RT (158–166)
Author Location Pol (337–345)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location RT (158–166)
Author Location Pol (313–321)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3, A11)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location RT (158–166)
Author Location Pol (325–333)
Epitope AIFQSSMTK
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A3, A11, A33)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- Variants (S/A)IFQSSMTK are specific for the A/B clades.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-A3 women, 2/2 HEPS and 3/3 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in one of the 2/2 HEPS cases and in one of the 3/3 HIV-1 infected women.

HXB2 Location RT (158–166)
Author Location Pol
Epitope AIFQSSMTK
Epitope name 1339
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3, A3.1, A11, A*6801, A33)
Donor MHC A02, A03, B08, B51, Cw01, Cw07; A03, A26, B08, B52, ?; A03, A11, B14, B05, Cw08
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, supertype, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for AIFQSSMTK: 59% Supertype epitope binding to A03, A3.1, A11, A6801, A33.

HXB2 Location RT (158–166)
Author Location RT (325–333)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3.1)
Keywords responses in children, mother-to-infant transmission
References Brander & Walker 1995

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.

HXB2 Location RT (158–166)
Author Location RT (325–333)
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A3.1)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was HLA A3 and reacted with this epitope as well as two other A3.1 epitopes.

HXB2 Location RT (158–166)
Author Location RT (325–333 LAI)
Epitope AIFQSSMTK
Subtype B
Immunogen
Species (MHC) human (A33)
References Rowland-Jones 1995

- Defined as minimal peptide by titration curve, S. Rowland-Jones, pers. comm.

HXB2 Location RT (158–166)
Author Location
Epitope AIFQSSMTK
Immunogen HIV-1 infection
Species (MHC) human (A33)

Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls, ML1668.

HXB2 Location RT (158–182)
Author Location RT (325–349 PV22)
Epitope AIFQSSMTKILEPFRKQNPDIVIYQ
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Jassoy *et al.* 1993

- HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.

HXB2 Location RT (158–182)
Author Location RT (325–349)
Epitope AIFQSSMTKILEPFRKQNPDIVIYQ
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Price *et al.* 1995

- Study of cytokines released by HIV-1 specific activated CTL.

HXB2 Location RT (164–172)
Author Location Pol (343–351)
Epitope MTKILEPFR
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 4/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location RT (173–181)
Author Location RT (173–181 LAI)
Epitope KQNPDIVIY
Subtype B
Immunogen
Species (MHC) human (A*3002)
Keywords optimal epitope
References Frahm *et al.* 2004; Goulder *et al.* 2001a

- C. Brander notes this is an A*3002 epitope.

HXB2 Location RT (173–181)
Author Location RT
Epitope KQNPDIVIY
Epitope name KY9 (RT-53)
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
References Goulder *et al.* 2001a

- HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule.
- A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood.
- Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean.
- In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant.
- In subject 199 four additional A*3002 epitopes were identified.
- Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)

HXB2 Location RT (173–181)
Author Location (C consensus)
Epitope AQNPEIVIY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location RT (175–183)
Author Location RT (328–336 IIIB)
Epitope NPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 1997

- A CTL clone responsive to this epitope was obtained.
- 3/7 B35-positive individuals had a CTL response to this epitope.
- D to E, or V to I, substitutions at positions 3 or 5, respectively, reduces CTL activity and binding to B*3501.

HXB2 Location RT (175–183)
Author Location RT (328–336 IIIB)
Epitope NPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*3501 epitope.

HXB2 Location RT (175–183)
Author Location RT (342–350 LAI)
Epitope HPDIVIYQY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*3501 epitope.

HXB2 Location RT (175–183)
Author Location Pol (330–338)
Epitope NPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 2000a
- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A.
- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals.
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm.
- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

HXB2 Location RT (175–183)
Author Location RT (175–183 IIIB)
Epitope NPDIVIYQY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords epitope processing, escape
References Moore *et al.* 2002b
- HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing.
- NPDIVIYQY was one of two epitopes characterized in detail. D177x substitutions are know to specifically abrogate binding to HLA-B*3501, and not other B*35 subtypes. D177x substitutions were associated with people who carried HLA-B*3501 and not other B*35 subtypes; considering high resolution typing generally strengthened the B*35 associations.

HXB2 Location RT (175–183)
Author Location RT (175–183)
Epitope NPDIVIYQY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Donor MHC A*2301, B*3501, B*1503 (B72), Cw2, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003
- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ INFγ T-cell responses in 21 men within 15-92days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFNγ secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location RT (175–183)
Author Location RT (342–350 LAI)
Epitope HPDIVIYQY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords review
References McMichael & Walker 1994
- Review of HIV CTL epitopes.

HXB2 Location RT (175–183)
Author Location RT (329–337)
Epitope HPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Rowland-Jones *et al.* 1995
- NPDIVIYQY preferred sequence for some CTL clones, HIV-2 NPDVILIQY is also recognized.

HXB2 Location RT (175–183)
Author Location (SF2)
Epitope NPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, rate of progression, escape
References Kawana *et al.* 1999

- HLA B35 is associated with rapid disease progression.
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals.
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation.
- npEiviyqy was found in 8/10 of the B35+ individuals, and two of the B35- individuals—the D–>E substituted peptide had reduced binding affinity to B35 and may be an escape mutant.

HXB2 Location RT (175–183)
Author Location RT (329–337)
Epitope HPDIVIYQY
Immunogen in vitro stimulation or selection
Species (MHC) human (B35)
References Lalvani *et al.* 1997

- A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers.
- This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors.

HXB2 Location RT (175–183)
Author Location RT (328–336 IIIB)
Epitope NPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Menendez-Arias *et al.* 1998; Shiga *et al.* 1996

- Binds HLA-B*3501.
- CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding Menendez-Arias *et al.* [1998]

HXB2 Location RT (175–183)
Author Location RT (328–336 IIIB)
Epitope NPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords review, escape
References Menendez-Arias *et al.* 1998; Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.
- NPDIIIYQY, a variant found in HIV-1 JRCSF, was also recognized.
- NPEIVIYQY, was also recognized.
- NPDLVIYQY, was also recognized.
- Menendez-Arias *et al.* [1998], in a review, notes that the YXDD motif, highly conserved among polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding.

HXB2 Location RT (175–183)
Author Location RT
Epitope NPDIVIYQY
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B35)
Keywords review, inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Menendez-Arias *et al.* 1998; Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A subtype consensus is HPDIVIYQY.
- The D subtype consensus is NPEIVIYQY.
- Menendez-Arias *et al.* [1998], in a review, notes that the YXDD motif, highly conserved among polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding.

HXB2 Location RT (175–183)
Author Location Pol (subtype B)
Epitope NPDIVIYQY
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B35)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- Clade A version of epitope HPDIVIYQY, Clade D NPEIVIYQY.

HXB2 Location RT (175–183)
Author Location Pol
Epitope HPDIVIYQY
Immunogen
Species (MHC) human (B35)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective.
- HIV-2 version of this epitope is not conserved: NPDVILIQY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also Rowland-Jones *et al.* [1995]

HXB2 Location RT (175–183)
Author Location
Epitope HPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location RT (175–183)
Author Location Pol (subtype A)
Epitope HPDIVIYQY
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- HPDIVIYQY or NPDIVIYQY was recognized in 1 of the 6 women (ML857), and the response was present in the last available sample prior to seroconversion, 7 months.
- 20/20 sequences of the infecting strain had three substitutions in this epitope, all 20 were NpQiIiyqy, and this form was not recognized by CTL from ML 857 – this was the only case in the study where a virus carrying an unrecognized form of the epitope broke through.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- NPDIVIYQY was recognized by 1/22 HEPS control sex workers, ML887.

HXB2 Location RT (175–183)
Author Location RT (175–183 SF2)
Epitope NPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 1/1 group 3.

HXB2 Location RT (175–183)
Author Location Pol (342–350)
Epitope HPDIVIYQY
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B35)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- Variants (H/N)PDIVIYQY are specific for the A/B clades.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B35 women, 2/3 HEPS and 1/4 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in only one of the 2/3 HEPS cases, and was not to this epitope in the one responsive HIV-1 infected women.
- Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion and the loss of the pre-seroconversion response was not due to sequence variation within these epitopes.

HXB2 Location RT (175–183)
Author Location
Epitope HPDIVIYQY
Epitope name Pol-HY9

Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B35, 4/21 (19%) recognized this epitope.

HXB2 Location RT (175–183)
Author Location Pol
Epitope NPDIVIYQY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Donor MHC A3, A11, B35, B51
Keywords mother-to-infant transmission
References Sabbaj *et al.* 2002a

- IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release.
- T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known B35 epitope NPDIVIYQY.
- The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.

HXB2 Location RT (175–183)
Author Location Pol
Epitope HPDIVIYQY
Subtype A
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human, macaque (B35)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location RT (175–183)
Author Location Pol (342–350)
Epitope HPDIVIYQY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- None of three patients responded to this peptide with GzB producing cells, while one of the patients responded with IFN-gamma producing cells.

HXB2 Location RT (175–183)
Author Location RT Pol (330–338)
Epitope HPDIVIYQY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/9 patients recognized this epitope.

HXB2 Location RT (175–184)
Author Location RT (175–184 LAI)
Epitope NPDIVIYQYM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B51)
References Samri *et al.* 2000

- This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors.
- Patient 246#1 (B51), was found by ELISPOT to recognize the wild type and the mutated peptide after zidovudine treatment.
- The resistance mutation M184V gave an increased predicted binding score to B51 (http://bimas.dcrt.nih.gov/molbio/hla_bind) compared to the wildtype RT sequence and also an increased ELISPOT reactivity.

HXB2 Location RT (175–199)
Author Location RT (342–366 LAI)
Epitope NPDIVIYQYMDDLYVGSDLEIGQHR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Menendez-Arias *et al.* 1998; Walker *et al.* 1989

- One of five epitopes defined for RT-specific CTL clones in this study.

HXB2 Location RT (179–187)
Author Location RT
Epitope VIYQYMDDL
Immunogen Vaccine
Vector/Type: vaccinia
Species (MHC) human (A*0201)
References Hanke *et al.* 1998a; Hanke *et al.* 1998b

- This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans.

HXB2 Location RT (179–187)
Author Location RT
Epitope VIYQYMDDL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Tan *et al.* 1999

- Adoptive transfer of two autologous *in vitro*-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts.
- Tetramer staining failed for the VIYQYMDDL epitope as the tetramer was unstable.

HXB2 Location RT (179–187)
Author Location Pol (346–354)
Epitope VIYQYMDDL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords epitope processing, immunodominance, escape
References Sewell *et al.* 1999

- Proteasome regulation influences epitope processing and could influence patterns of immunodominance.
- The proteasome is inhibited by lactacystin treatment, and gamma IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome.
- IFN-gamma induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways.
- ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway.
- This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants.

HXB2 Location RT (179–187)
Author Location RT (346–354 LAI)
Epitope VIYQYMDDL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords review
References Harrer *et al.* 1996a; Menendez-Arias *et al.* 1998

- The substitution VIYQYVDDL abrogates CTL response and confers drug resistance.
- Menendez-Arias *et al.* [1998], in a review, notes that this epitope includes catalytic residues (Asp-185 and Asp-186) in the active site of RT.

HXB2 Location RT (179–187)
Author Location RT (346–354 LAI)
Epitope VIYQYMDDL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0201 epitope.

HXB2 Location RT (179–187)
Author Location RT (346–354)
Epitope VIYQYMDDL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords review, escape
References Brander *et al.* 1998a; Menendez-Arias *et al.* 1998

- Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape.
- Only one subject had CTL against all three epitopes.
- Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area.
- In the review Menendez-Arias *et al.* [1998] the authors note that substitution of three residues in this epitope can confer resistance to RT inhibitors (1, 3, and 6) – substitutions V1E and M6V abolish CTL activity, and M6V confers resistance to 3TC – substitution Y3C reduces CTL activity and is associated with resistance to non-nucleoside RT inhibitors.

HXB2 Location RT (179–187)
Author Location RT
Epitope VIYQYMDDL
Epitope name RT VL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)

Keywords inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, including RT VL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- RT VL9 was not recognized by any of the 22 HLA-A2 patients with chronic HIV-1 infection or the 13 HLA-A2 patients with acute HIV-1 infection included in this study.

HXB2 Location RT (179–187)
Author Location RT (346–354)
Epitope VIYQYMDDL
Epitope name VL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Dela Cruz *et al.* 2000

- Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL.
- These antigens could also be used to stimulate primary responses *in vitro*.

HXB2 Location RT (179–187)
Author Location Pol (346–354)
Epitope VIYQYMDDL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords epitope processing, immunodominance
References Sewell *et al.* 2002

- Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing.
- ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.

HXB2 Location RT (179–187)
Author Location Pol
Epitope VIYQYMDDL
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human, macaque (A*0201)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location RT (179–187)
Author Location RT (179–187)
Epitope VIYQYMDDL
Subtype B
Immunogen Vaccine
Vector/Type: peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12
Species (MHC) mouse (A*0201)
Donor MHC A2.1
Assay type cytokine production, Chromium-release assay
Keywords binding affinity, vaccine-induced epitopes
References Okazaki *et al.* 2003

- Alanine substitutions of VIYQYMDDL were tested for importance of each amino acid for HLA-A2.1 binding. Peptide variant (vLyqymddV) showed an 8 fold higher MHC binding affinity than wild type. YLyqymddV had an even higher binding affinity, but the Y at position one blocked TCR recognition. The higher affinity form of vLyqymddV induced CTL *in vivo* that could protect against a vaccinia virus expressing RT and the wild type epitope.

HXB2 Location RT (179–187)
Author Location RT (179–187 MN)
Epitope VIYQYMDDL
Subtype B
Immunogen Vaccine
Vector/Type: DNA, polyepitope *Strain:* B clade MN *HIV component:* gp120, Protease, RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) humanized mouse (A*0201)

Assay type CD8 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance, immunotherapy
References Isaguliants *et al.* 2004

- Immunization of HLA-A*0201-transgenic mice with synthetic genes encoding clusters of human A*0201 CTL epitopes located at the sites of drug resistance mutations, induced RT-specific cellular responses indicating the immunogenicity of these constructs. This vaccine strategy may be a first step towards a therapeutic vaccine against drug-resistant strains.
- This was one of five HLA-A*0201 epitopes from the RT or protease proteins that was included in the polyepitope vaccine. When the transgenic HLA A*0202 mice were vaccinated with the polyepitope construct or with a mixture of RT peptides, a sustained low level CD8+ T-cell gamma IFN response was observed, in contrast to when an intact RT gene was used for vaccination.

HXB2 Location RT (179–187)
Author Location Pol (346–354)
Epitope VIYQYMDDL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- One of seven patients responded to this peptide with GzB producing cells, while none of the patients responded with IFN-gamma producing cells.

HXB2 Location RT (179–187)
Author Location RT
Epitope VIYQYMMDL
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A and D consensus sequences are both VIYQYMMDL.

HXB2 Location RT (179–187)
Author Location Pol (346–354)
Epitope VIYQYMDDL
Immunogen Vaccine
Vector/Type: DNA prime with vaccinia boost
Species (MHC) human (A2)
References Woodberry *et al.* 1999

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice.
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- VIYQYMDDL was recognized by 3 of the HLA-A2 patients.

HXB2 Location RT (179–187)
Author Location RT (179–187)
Epitope VIYQYMDDL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords escape, immunotherapy
References Schmitt *et al.* 2000

- The mutation M184V confers resistance to lamivudine, and is in the middle of the HLA-A2 epitope VIYQYMDDL.
- 1/28 individuals tested produced HIV-1 RT-specific CTL that recognized the peptide representing the lamivudine escape mutants VIYQYVDDL and VIYQYIDDL, but failed to recognize the wildtype epitope VIYQYMDDL.
- This suggests immunotherapy stimulating anti-VIYQYVDDL responses maybe helpful for reducing lamivudine escape.

HXB2 Location RT (179–187)
Author Location RT (179–187)
Epitope VIYQYMDDL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)

HXB2 Location RT (179–187)
Author Location Pol (339–347 93TH253 subtype CRF01)
Epitope VIYQYMDDL
Epitope name P334-342
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HIV exposed persistently seronegative (HEPS)

References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.

HXB2 Location RT (179–187)
Author Location Pol (339–347 93TH253 subtype CRF01)
Epitope VIYQYMDDL
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 2/4 tested FSWs recognized the E clade version of this epitope, which is identical to the previously defined B clade version VIYQYMDDL.
- This epitope was conserved in many subtypes, and exact matches were very uncommon.

HXB2 Location RT (179–187)
Author Location RT (179–187)
Epitope VIYQYMDDL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

HXB2 Location RT (179–187)
Author Location Pol (346–354 LAI)
Epitope VIYQYMDDL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, epitope processing
References Kelleher *et al.* 2001a

- Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in an intracellular context.
- RTV did not alter the presentation two RT A2 epitopes processed by distinct pathways: ILKEPVHGV, generated by the constitutive proteasome containing the MB1 beta subunit, and VIYQYMDDL which is dependent on IFNgamma induction of LMP7 which replaces MB1 in the immunoproteasome, and is destroyed by MB1 in the constitutive proteasome.
- RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.

HXB2 Location RT (179–187)
Author Location Pol (334–)
Epitope VIYQYMDDL
Epitope name Pol334
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This epitope was one of the previously identified HLA-A2 epitopes studied.
- 1/17 HIV-infected HLA-A2+ people in this study recognized this epitope.

HXB2 Location RT (179–187)
Author Location Pol (334–342)
Epitope VIYQYMDDL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A02, B35, Bw62
Assay type proliferation, Chromium-release assay, Flow cytometric CTL assay
Keywords HAART, ART, memory cells, immune dysfunction
References Gamberg *et al.* 2004a

- HAART restores HIV specific immunity after advanced infection by increase of CD4+ and CD8+ T cell numbers after supression of viral replication. However, HIV specific CTLs emerged only with detectable viral replication breakthroughs and were short-lived while CD4+ T-cell responses remained compromised, suggesting failure of generating stable CD8+ memory T-cells in the absence of HIV-specific T-helper responses.

HXB2 Location RT (179–187)
Author Location RT (179–187)
Epitope VIYQYMDDL
Subtype B
Immunogen HIV-1 infection

Species (MHC) human (A2)
Country Canada.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords HAART, ART, immunotherapy, variant cross-recognition or cross-neutralization
References Mason *et al.* 2004

- Accumulation of specific antiretroviral drug-resistance mutations in Pol gene was shown to sustain and even enhance the antigenicity and immunogenicity of HIV-1 CTL epitopes in this region. Several different patterns of cross-reactivity and selective recognition of wild-type and variant epitopes were found.
- VIcQYMDDL, VIYQYvDDL and VIcQYvDDL variants are detected due to appearence of Y181C and M184V resistance mutations. The double mutant was the only form recognized in one A02 treated individual, the epitope was not recognized in another.

HXB2 Location RT (179–187)
Author Location RT Pol (334–342)
Epitope VIYQYNDDL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/19 patients recognized this epitope.

HXB2 Location RT (179–187)
Author Location Pol
Epitope VIYQMDDL
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2)
Donor MHC A02, A30, B4402, B15
Assay type Tetramer binding, T-cell Elispot
Keywords HIV exposed persistently seronegative (HEPS)
References Missale *et al.* 2004

- HIV-specific T-cell response was tested in HIV-uninfected patients exposed to blood from a patient with highly replicating HIV; these same patients were nosocomially infected with HBV. HIV-specific T-cell responses were directed to structural and non-structural HIV proteins in two patients suggesting that the virus replicated in these patients sufficiently to prime a cell-mediated immune response that protected these individuals from HIV infection.
- This patient responded to 4/8 HIV epitopes tested in an IFNgamma EliSpot assay or tetramer assay. Responses were detected 8 and 28 weeks after exposure. No response to this epitope was detected by IFNgamma EliSpot, but a response was detected by tetramer staining.

HXB2 Location RT (179–187)
Author Location Pol (subtype B)
Epitope VIYQYMMDL
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2, A*0202)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among A, B and D clade viruses.

HXB2 Location RT (179–187)
Author Location RT (346–354 LAI)
Epitope VIYQYMDDL
Epitope name LR26
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG
Species (MHC) mouse (A2.1)
Keywords binding affinity, vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2001

- The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01).
- The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.
- HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants.
- All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.

HXB2 Location RT (179–187)
Author Location RT (346–354 LAI)
Epitope VIYQYMDDL
Epitope name LR26
Subtype B

Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI
Adjuvant: Incomplete Freund's Adjuvant (IFA), IL-12, P30
Species (MHC) mouse (A2.1)
Keywords vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2002

- When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination Peter *et al.* [2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.

HXB2 Location RT (180–189)
Author Location RT (LAI)
Epitope IYQYMDDLYV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Menendez-Arias *et al.* 1998; van der Burg *et al.* 1997

- Recognized by CTL from a progressor, spans important RT functional domain.
- A previous study determined that this was an epitope recognized by a long-term survivor.

HXB2 Location RT (181–189)
Author Location RT (181–189 LAI)
Epitope YQYMDDLYV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity, computational epitope prediction
References Samri *et al.* 2000

- This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors.
- High levels of recognition by ELISPOT were observed for zidovudine induced mutation YQYVDDLYV and for the wild-type peptide YQYMDDLYV in patient 250#0 (HLA-A*0201), but neither were recognized by patient 201#5 (also HLA-A*0201)
- Both the wild-type and the mutated peptide were computer predicted to have a high binding affinity for A2 (http//bimas.dcrt.nih.gov/molbio/hla_bind)

HXB2 Location RT (192–201)
Author Location RT (192–201)
Epitope DLEIGQHRTK
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules.

HXB2 Location RT (192–201)
Author Location Pol (192–201)
Epitope DLEIGQHRTK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 7 epitopes from this individual that varied over time, although the internal mutations did not become fixed. The dleMgqhrtk variant arose at late time points.

HXB2 Location RT (192–216)
Author Location RT (359–383 HXB2)
Epitope DLEIGQHRTKIEELRQHLLRWGLTT
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Bw60)
References Menendez-Arias *et al.* 1998; Walker *et al.* 1989

- One of five epitopes defined for RT-specific CTL clones in this study.

HXB2 Location RT (192–216)
Author Location RT (191–215)
Epitope DLEIGQHRTKIEELRQHLLRWGFTT
Immunogen HIV-1 infection
Species (MHC) human (polyclonal)
Keywords HAART, ART, escape
References Haas *et al.* 1997; Menendez-Arias *et al.* 1998

- Polyclonal CTL recognition switched from RT 191-215 to RT 514-524 when AZT therapy selected for the resistance mutation, and presumably the escape variant, RT T215Y.

HXB2 Location RT (198–212)
Author Location RT (SF2)
Epitope HRTKIEELRQHLLRW
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.
- The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.

HXB2 Location RT (201–209)
Author Location RT (201–209)
Epitope KIEELRQHL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules.

HXB2 Location RT (201–210)
Author Location Pol
Epitope KIEELRQHLL
Immunogen
Species (MHC) human (B58)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay.
- KIEELRQHLL was newly identified as a HLA-B58 epitope in this study, it had been previously shown to be presented by HLA-A2 and Bw60.
- KIEELRQHLL did not bind detectably to B7.

HXB2 Location RT (202–210)
Author Location RT (202–210 LAI)
Epitope IEELRQHLL
Subtype B
Immunogen
Species (MHC) human (B*4001)
Keywords optimal epitope
References Altfeld *et al.* 2000; Frahm *et al.* 2004

- C. Brander notes this is a B*4001 epitope.

HXB2 Location RT (202–210)
Author Location RT (SF2)
Epitope IEELRQHLL
Immunogen HIV-1 infection
Species (MHC) human (B60)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with preseroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 1/1 group 2, and 0/0 group 3.

HXB2 Location RT (202–210)
Author Location RT
Epitope IEELRQHLL
Epitope name IL9
Immunogen HIV-1 infection
Species (MHC) human (B60)
Donor MHC A2, A24, B38, B60, Cw2, Cw12
Assay type CD8 T-cell Elispot - IFNγ
Keywords HAART, ART, supervised treatment interruptions (STI), early treatment
References Montefiori *et al.* 2003

- HIV-1 + patient AC10 underwent early HAART treatment, which was discontinued 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.

HXB2 Location RT (202–210)
Author Location RT (SF2)
Epitope IEELRQHLL
Immunogen HIV-1 infection
Species (MHC) human (B60, B*4001)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes.
- B60 is present in 10-20% of the Caucasoid and very common in Asian populations.

HXB2 Location RT (202–210)
Author Location RT (202–210)
Epitope IEELRQHLL
Immunogen HIV-1 infection
Species (MHC) human (B60, B61)
Keywords immunodominance
References Day *et al.* 2001

- No immunodominant responses were detected to five B61-restricted epitopes tested.
- All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response.

HXB2 Location RT (203–211)
Author Location RT
Epitope EELRQHLLR
Immunogen HIV-1 infection
Species (MHC) human (B44)
Donor MHC A*3101, A68, B*4403, B51
Keywords HAART, ART, supervised treatment interruptions (STI)
References Arnedo-Valero *et al.* 2004

- T cell immune responses following STI were monitored in two chronically HIV-1 infected partners (A and B) who had contracted HIV-1 during 1992. Both were heterozygous for the CCR5 delta32, and had different HLAs and treatment histories. STI induced strong transitory CD4+ and CD8+ T cell responses in both patients. Patient A displayed broad CD8+ T cell responses directed against Env, Pol, Gag, and Nef HIV-1 antigens. CTL responses in patient B were mainly directed against two epitopes: Gag(p24)NANPDSKTI and Pol(RT)EELRQHLLRW.
- Despite the host differences, both patients had similar dynamics of vial evolution and CD4+ T-cells, suggesting that good immune reponses to STI may be more related to the virus than host characteristics in these cases.

HXB2 Location RT (203–212)
Author Location RT (LAI)
Epitope EELRQHLLRW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Menendez-Arias *et al.* 1998; van der Burg *et al.* 1997

- The only epitope recognized by CTL from a long-term survivor in two samples taken six years apart.
- Recognized by CTL from a progressor, EILKEPVGHGV and TWETWWTEYW were also recognized.

HXB2 Location RT (203–212)
Author Location RT (203–212)
Epitope EELRQHLLRW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44)
Country Canada.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords HAART, ART, immunotherapy, variant cross-recognition or cross-neutralization
References Mason *et al.* 2004

- Accumulation of specific antiretroviral drug-resistance mutations in Pol gene was shown to sustain and even enhance the antigenicity and immunogenicity of HIV-1 CTL epitopes in this region. Several different patterns of cross-reactivity and selective recognition of wild-type and variant epitopes were found.
- EELRQHLwRW variant is detected due to appearence of L210W resistance mutation. The in this case, the wild-type epitope was preferentially recognized relative to the L210W variant.

HXB2 Location RT (203–212)
Author Location RT Pol (358–367)
Epitope EELRQHLLRW
Immunogen HIV-1 infection
Species (MHC) human (B44)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 9/11 patients recognized this epitope; of three B*44 eptiopes tested, this was the only one that was recognized by more than 2/11 patients.

HXB2 Location RT (203–212)
Author Location RT
Epitope EELRQHLLRW
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B44)
Donor MHC A01, A03, B39, B44, Cw4, Cw6
Assay type T-cell Elispot
Keywords HIV exposed persistently seronegative (HEPS)
References Missale *et al.* 2004

- HIV-specific T-cell response was tested in HIV-uninfected patients exposed to blood from a patient with highly replicating HIV; these same patients were nosocomially infected with HBV. HIV-specific T-cell responses were directed to structural and non-structural HIV proteins in two patients suggesting that the virus replicated in these patients sufficiently to prime a cell-mediated immune response that protected these individuals from HIV infection.
- This patient responded to 3/11 HIV epitopes tested in an IFNgamma EliSpot assay. Responses were detected 16 and 20 weeks after exposure, but were lost by week 80.

HXB2 Location RT (209–220)
Author Location RT (209–220 MN)
Epitope LLRWGLTTPDKK
Subtype B
Immunogen Vaccine
Vector/Type: DNA, polyepitope *Strain:* B clade MN *HIV component:* gp120, Protease, RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) humanized mouse (A*0201)
Assay type CD8 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance, immunotherapy
References Isaguliants *et al.* 2004

- Immunization of HLA-A*0201-transgenic mice with synthetic genes encoding clusters of human A*0201 CTL epitopes located at the sites of drug resistance mutations, induced RT-specific cellular responses indicating the immunogenicity of these constructs. This vaccine strategy may be a first step towards a therapeutic vaccine against drug-resistant strains.
- This was one of five HLA-A*0201 epitopes from the RT or protease proteins that was included in the polyepitope vaccine. When the transgenic HLA A*0202 mice were vaccinated with the polyepitope construct or with a mixture of RT peptides,

a sustained low level CD8+ T-cell gamma IFN response was observed, in contrast to when an intact RT gene was used for vaccination.

HXB2 Location RT (209–220)
Author Location RT (209–220)
Epitope LLRWGLTTPDKK
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules.

HXB2 Location RT (214–223)
Author Location Pol
Epitope FTTPDKKHQK
Epitope name 1267
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A11, A68)
Donor MHC A11, A68, B42, B45, Cw16, Cw17
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, supertype, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for FTTPDKKHQK:36% Supertype epitope binding to A68 and A11.

HXB2 Location RT (215–224)
Author Location Pol
Epitope TTPDKKHQKE
Epitope name 1281
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A11)
Donor MHC A11, A68, B42, B45, Cw16, Cw17; A01, A68, B15, B40, Cw03
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, supertype, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for TTPDKKHQKE:60% Supertype epitope binding to A68.

HXB2 Location RT (240–257)
Author Location RT (240–257 HXB2)
Epitope TVQPIVLPEKDSWTVNDI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location RT (243–252)
Author Location RT (LAI)
Epitope PIVLPEKDSW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
References Menendez-Arias *et al.* 1998; van der Burg *et al.* 1997

- Recognized by CTL from a progressor and a long-term survivor, KITTESIVIW was also recognized.

HXB2 Location RT (243–252)
Author Location RT (LAI)
Epitope PIVLPEKDSW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords binding affinity, escape

References Menendez-Arias *et al.* 1998; van der Burg *et al.* 1997

- Recognized by CTL from long-term survivor, whose CTL response persisted for more than 10 years – the substitution V3M reduced affinity but was well recognized, on the other hand V3T and D8G did not reduce affinity, but abrogated CTL response.

HXB2 Location RT (243–252)
Author Location RT (410–419)
Epitope PIVLPEKDSW
Epitope name PIV
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- None of the 8 study subjects recognized this epitope but none were HLA B57+

HXB2 Location RT (243–252)
Author Location RT
Epitope PIVLPEKDSW
Epitope name PIV
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location RT (243–252)
Author Location RT Pol (398–407)
Epitope PIVLPEKDSW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 6/7 patients recognized this epitope.

HXB2 Location RT (244–252)
Author Location RT (399–407)
Epitope IVLPEKDSW
Immunogen
Species (MHC) human (B*5701)
Keywords optimal epitope
References Frahm *et al.* 2004

- Subtype of B57 not determined.
- C. Brander notes this is a B*5701 epitope.

HXB2 Location RT (244–252)
Author Location RT (244–252 LAI)
Epitope IVLPEKDSW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701, B*5801)
Keywords binding affinity, rate of progression, escape
References Klein *et al.* 1998

- This peptide was defined as the optimal epitope.
- B57 has been associated with long-term non-progression in the Amsterdam cohort.
- The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag.
- B57 restricted CTL responses are targeted at multiple proteins, but one LTS had a response that was dominated by reactivity to the epitope – two variants were found in this LTS: ITLPEKESW, which bound to B*5701 with similar affinity as the index peptide but was an escape mutant that was not recognized by CTL, and IMLPEKDSW, which bound to B*5701 with reduced affinity but could still be recognized.
- In an additional HIV+ LTS, only the variant IELPEKDSW was found, and this epitope was recognized by CTL but had less affinity for B*5701 than the index peptide.
- This epitope was recognized in the context of both HLA-B*5701 and B*5801.

HXB2 Location RT (244–252)
Author Location Pol (244–252)
Epitope IVLPEKDSW
Immunogen HIV-1 infection
Species (MHC) human (B*5801)
References Appay *et al.* 2000

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

HXB2 Location RT (244–252)
Author Location RT (399–407)
Epitope IVLPEKDSW

Immunogen
Species (MHC) human (B57)
References van der Burg *et al.* 1997

HXB2 Location RT (244–252)
Author Location RT (244–252)
Epitope IVLPEKDSW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords early-expressed proteins, kinetics
References Guillon *et al.* 2002b

- An early-expressed Nef protein was modified to contain Env and Pol epitopes to enable the study the effect of expression kinetics on CTL mediated suppression of replication. The "EpiNef" construct was inserted into a recombinant vaccinia virus which was used to infect a target cell line; the target cells were lysed by CTL clones specific for the Env and Pol epitopes indicating that they were properly processed.

HXB2 Location RT (244–252)
Author Location RT (244–252 ACH320.2A.2.1)
Epitope IVLPEKDSW
Subtype B
Immunogen HIV-1 infection
Species (MHC) (B57)
Keywords acute infection, early-expressed proteins, kinetics
References van Baalen *et al.* 2002

- Tat, Rev and Nef are the first HIV proteins expressed upon acute infection of T-cells (< 6 hours), and RT is not expressed until after 24 hours. The B14-restricted Rev-SAEPVPLQL specific CD8 T-cell clone TCC108, and the B57-restricted RT-IVLPEKDSW specific CD8 T-cell clone TCL1C11 were co-incubated with CD4+ cultures innoculated with HIV-1 at low MOI. Co-incubation with the Rev-specific CTL resulted in two logs less HIV-1 production in ten days of culture. When the RT epitope was cloned into the Nef gene of the infecting strain, another early expressed protein, it proved as effective as the Rev epitope at inhibiting viral production. A mathematical model of CTL-target interactions suggest early proteins are important for vaccine design.

HXB2 Location RT (245–252)
Author Location Pol
Epitope IVPEKDSW
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Kostense *et al.* 2001

- HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load.
- Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional.
- In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival.

HXB2 Location RT (259–267)
Author Location Pol
Epitope KLVGKLNWA
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).
- Tetramer staining with A2, beta2microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific sells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population.

HXB2 Location RT (260–271)
Author Location RT (415–426 IIIB)
Epitope LVGKLNWASQIY
Immunogen HIV-1 infection
Species (MHC) human (B*1501)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*1501 epitope.

HXB2 Location RT (260–271)
Author Location Pol (260–271)
Epitope LVGKLNWASQIY
Immunogen HIV-1 infection
Species (MHC) human (B15)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 7 epitopes from this individual that varied over time, although the internal mutations did not become fixed. lvgkXnwasqiy variants arose at late time points

HXB2 Location RT (260–271)
Author Location RT (260–271)
Epitope LVGKLNWASQIY
Immunogen HIV-1 infection
Species (MHC) human (B62)

Keywords immunodominance
References Day *et al.* 2001

- No immunodominant responses were detected to four B62-restricted epitopes tested.

HXB2 Location RT (260–271)
Author Location RT (415–426 IIIB)
Epitope LVGKLNWASQIY
Immunogen HIV-1 infection
Species (MHC) human (Bw62)
References Brander & Walker 1996; Menendez-Arias *et al.* 1998

- P. Johnson, pers. comm.

HXB2 Location RT (263–271)
Author Location RT (263–271 LAI)
Epitope KLNWASQIY
Subtype B
Immunogen
Species (MHC) human (A*3002)
Keywords optimal epitope
References Frahm *et al.* 2004; Goulder *et al.* 2001a

- C. Brander notes this is an A*3002 epitope.

HXB2 Location RT (263–271)
Author Location RT
Epitope KLNWASQIY
Epitope name KY9 (RT-35)
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
References Goulder *et al.* 2001a

- HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule.
- A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood.
- Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean.
- In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant.
- In subject 199 four additional A*3002 epitopes were identified.
- Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)

HXB2 Location RT (263–271)
Author Location (C consensus)
Epitope KLNWASQIY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location RT (263–271)
Author Location RT
Epitope KLNWASQIY
Epitope name A30-KY11(RT)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A30)
Donor MHC A30, A32, B18, B27
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).

HXB2 Location RT (266–285)
Author Location Pol (421–440)
Epitope WASQIYPGIKVRQLCKLLRG
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.

- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location RT (268–282)
Author Location RT (SF2)
Epitope SQIYPGIKVRQLCKL
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2001a

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- RT peptides SQIYPGIKVRQLCKL and WKGSPAIFQSSMTKI were recognized.

HXB2 Location RT (269–277)
Author Location Pol (424–432)
Epitope QIYAGIKVK
Subtype B, CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords binding affinity, inter-clade comparisons
References Fukada *et al.* 2002

- binding affinity, inter-clade comparisons.
- Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals.
- QIYAGIKVK is commonly found in viruses representing subtypes A, B and E. It was strongly recognized by CTL from 1/5 B clade infected Japanese subjects, and 5/7 E clade infected Thai subjects.
- QIYAGIKVK had the highest A*1101 binding affinity, but qiyagikvR and qiyPgikvR (the most common C and D clade variant both bound to A*1101). QIYAGIKVK and qiyagikvR were both cross-presented by a clone from a B clade infection, but qiyPgikvR was not.

HXB2 Location RT (269–277)
Author Location (B consensus)
Epitope QIYAGIKVK
Epitope name QVK9
Immunogen HIV-1 infection
Species (MHC) human (A11)
Donor MHC A02, A11, B18, B44, Cw5, Cw12
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location RT (269–277)
Author Location (LAI)
Epitope QIYPGIKVR
Subtype B
Immunogen
Species (MHC) (A3)
Keywords optimal epitope
References Altfeld 2000; Frahm *et al.* 2004

HXB2 Location RT (269–277)
Author Location RT (269–277)
Epitope QIYPGIKVR
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.

HXB2 Location RT (269–277)
Author Location RT (424–432)
Epitope QIYPGIKVR
Epitope name A3-QR9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.

- 1/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 4/7 individuals began to have detectable responses to this epitope after STI.

HXB2 Location RT (269–277)
Author Location RT (269–277)
Epitope QIYAGIKVK
Epitope name A3-QR9 Pol
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant qiyagikvR. The initial CTL response to both variants was strong but eventually declined, particularly to the variant in the second strain. .

HXB2 Location RT (269–277)
Author Location RT (269–277)
Epitope QIYPGIKVR
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location RT (271–279)
Author Location (LAI)
Epitope YPGIKVRQL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4201 epitope.

HXB2 Location RT (271–279)
Author Location (C consensus)
Epitope YPGIKVRQL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*4201)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location RT (271–279)
Author Location RT (438–446 IIIB)
Epitope YPGIKVRQL
Immunogen HIV-1 infection
Species (MHC) human (B42)
Keywords responses in children, mother-to-infant transmission
References Menendez-Arias *et al.* 1998; Wilson *et al.* 1996

- YAGIKVRQL and YPGIKVKQL are naturally occurring variants that are both reactive.
- YHKIKVRQL is a naturally occurring variant that has not been tested.
- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.

HXB2 Location RT (271–279)
Author Location Pol (438–446 IIIB)
Epitope YPGIKVRQL
Immunogen HIV-1 infection
Species (MHC) human (B42)
Keywords mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- An additional variant that gave a positive CTL response: YPGIKVKQL, YAGIKVRQL.
- YHGIKVRQL was an escape mutant.

HXB2 Location RT (293–301)
Author Location RT (448–456 SF2)
Epitope IPLTEEAEL
Immunogen HIV-1 infection
Species (MHC) human (B*3501)

References Menendez-Arias *et al.* 1998; Tomiyama *et al.* 1997

- A CTL clone responsive to this epitope was obtained.
- Only 1/7 B35-positive individuals had a CTL response to this epitope.
- An E to K substitution at position 5 abrogates specific lysis, but not binding to B*3501.
- An I to V substitution at position 1, P to Q at position 2, and E to K at 5, abrogates specific lysis and binding to B*3501.
- An I to V substitution at position 1 did not alter reactivity.
- Reviewed in Menendez-Arias *et al.* [1998], this epitope lies in the thumb region of RT.

HXB2 Location RT (293–301)
Author Location Pol (HXB2, LAI)
Epitope IPLTEEAEL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Donor MHC A*2402, A*2601, B*3501, B5101
Country Japan.
Assay type cytokine production, Tetramer binding, Chromium-release assay
Keywords binding affinity, kinetics, TCR usage, characterizing CD8+ T cell responses, immune dysfunction
References Ueno *et al.* 2004b

- Two different clonotypes of CD8+ T-cells with specificity for this epitope were isolated from a chronic HIV+ patient. The clonotype with the relatively high affinity TCR had no cytolytic activity, cytokine production or proliferation in response to HIV-infected cells, while the moderate affinity clonotype had strong reactions. More than 3-fold increased duration in tetramer 1/2 life was observed with the defective clonotype. The TCRs from the two clonotypes preserved the phenotype when transduced into primary CD8+ T cells, suggesting the TCR with higher affinity was directly associated with impaired T-cell reactivity of the cells.
- The high affinity impared TCR was Valpha1.1/Vbeta13.3, the moderate affinity active TCR was Valpha12.1/Vbeta5.6.

HXB2 Location RT (293–301)
Author Location Pol (HXB2, LAI)
Epitope IPLTEEAEL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*3501, B*1501)
Donor MHC A*2402, A*2601, B*3501, B*5101
Country Japan.
Assay type cytokine production, Tetramer binding, Chromium-release assay
Keywords binding affinity, cross-presentation by different HLA, immunotherapy, TCR usage, characterizing CD8+ T cell responses
References Ueno *et al.* 2004a

- This paper described the transduction of HIV specific clone TCR genes Valpha12.1/Vbeta5.6 into primary CD8+ T cells. Epitope fine specificity and appropriate effector functions were observed in the transduced cells, although functional avidity could change due to different densities of TCR on the surface of the transduced cells. No allogenic responses were detected. This methodology could have immunotherapeutic applications.

HXB2 Location RT (293–301)
Author Location Pol (448–456 SF2-24)
Epitope IPLTEEAEL
Epitope name HIV-B35-SF2-24
Immunogen HIV-1 infection
Species (MHC) human (B*3501, B*5101)
References Tomiyama *et al.* 2000b

- This epitope is naturally processed and presented by both HLA-B*3501 and HLA-B*5101 and is cross-recognized by a single CTL clone.
- IPLTEEAEL binds approximately four times more tightly to HLA-B*3501 than HLA-B*5101.

HXB2 Location RT (293–301)
Author Location Pol (489–456)
Epitope IPLTEEAEL
Immunogen HIV-1 infection
Species (MHC) human (B*3501, B*5301, B*5101, B*0702)
Donor MHC A24/A26, B35/B51, Cw3/-
Keywords supertype, cross-presentation by different HLA, TCR usage
References Ueno *et al.* 2002

- The IPLTEEAEL epitope was known to be presented by both HLA-B*3501 and -B*5101 to a dual specific CTL clone. A single TCR complex bearing Valpha12.1 and Vβ5.6 was shown recognize the epitope in either HLA-B*3501 and -B*5101. Furthermore, this TCR also recognized the peptide presented by B*5301 and B*0702 in cytolytic CTL assays, demonstrating that this single TCR complex recognizes the same peptide presented by a range of HLA class I molecules.

HXB2 Location RT (293–301)
Author Location (SF2)
Epitope IPLTEEAEL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords rate of progression
References Kawana *et al.* 1999

- HLA B35 is associated with rapid disease progression.
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals.
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals but this was one of the six that had no B35 associated pattern of mutation.

HXB2 Location RT (293–301)
Author Location RT (448–456 SF2)
Epitope IPLTEEAEL
Immunogen HIV-1 infection
Species (MHC) human (B35, B51)
References Menendez-Arias *et al.* 1998; Shiga *et al.* 1996

- Binds HLA-B*3501 and B*5101.
- Reviewed in Menendez-Arias *et al.* [1998], this epitope lies in the thumb region of RT.

HXB2 Location RT (293–301)

Author Location Pol (447–455)
Epitope IPLTEEAEL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B51)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location RT (293–301)
Author Location RT (293–301)
Epitope IPLTEEAEL
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location RT (293–301)
Author Location RT Pol (286–294)
Epitope IPLTEEAEL
Epitope name IPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, Tetramer binding, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, immunodominance, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- The IPL epitope was found to be under positive selection for escape mutations and it was replaced by first variant between days 297 and 369, ipltGeael. This new variant was subsequently replaced by 2 further variants, that were even more resistent to CD8+ T cell recognition between days 369 and 635, ipltAeael and ipltVeael.

HXB2 Location RT (294–318)
Author Location RT (461–485 HXB2)
Epitope PLTEEAELELAENREILKEPVHGVY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Menendez-Arias *et al.* 1998; Walker *et al.* 1989

- One of five epitopes defined for RT-specific CTL clones in this study.

HXB2 Location RT (298–312)
Author Location RT (291–305)
Epitope EAELELAENREILKE
Epitope name EAE
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This was one of 8 reactive peptides found not to vary over time. It was one of four epitopes that were not precisely defined.

HXB2 Location RT (308–317)
Author Location RT (LAI)
Epitope EILKEPVGHV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Menendez-Arias *et al.* 1998; van der Burg *et al.* 1997

- Recognized by CTL from a long-term survivor, SPIETVPVKL was also recognized.
- Recognized by CTL from a progressor, EELRQHLLRW and TWETWWTEYW were also recognized.

HXB2 Location RT (309–317)
Author Location RT (476–484 LAI)
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*0201
Keywords HAART, ART, responses in children
References Luzuriaga *et al.* 2000

- Longitudinal study of 8 infants with prolonged viral suppression due to combination antiretroviral therapy showed no HIV-1 specific CTL responses in peripheral blood cells. 6/8 were studied using a Chromium release assay and no response was detected using Gag expressed in vaccinia in the target cells. Three HLA-A*0201 children were tested using SLYNTVATL or ILKEPVHGV HLA A*0201 tetramers and again no HIV-specific response was detected, either using PBMC specimens, or PBMC which had been stimulated *in vitro* for a week.
- In contrast, one of the children with suppressed HIV viral replication who was co-infected with HIV and EBV, while HIV-tetramer negative, had EBV-tetramer staining cells at a frequency of 0.14% in the PBMC.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords HAART, ART
References Huang *et al.* 2000

- The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed.
- Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords HAART, ART
References Rinaldo *et al.* 2000

- Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that persist after therapy and long periods of virus being below the level of detection.

HXB2 Location RT (309–317)
Author Location RT
Epitope ILKEPVHGV
Epitope name IV9
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords HAART, ART, immunodominance
References Scott-Algara *et al.* 2001

- This study examined with CTL response in HLA A*02+ children by tetramer staining for HLA-A2 immunodominant epitopes SLYNTVATL and ILKEPVHGV.
- 71% of the 28 HIV-1 infected HLA-A*02 positive children recognized both epitopes, with cells from 26 children stained positive by the gag tetramer (SLYNTVATL) and 21 children by the pol tetramer (ILKEPVHGV)
- There were no differences observed in children that had therapy versus those that did not.
- Tetramer-binding cells were memory activated CD28-, CD45RO+, CD45RA- HLADR+, CD69-, CD8+ T-cells.

HXB2 Location RT (309–317)
Author Location
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T cells and viral load.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Spiegel *et al.* 2000

- High levels of CD8+ HIV-1 specific and cytomegalovirus specific CTL were detected by HLA-A*0201-peptide tetramers in 3 infected subjects with very low CD4 counts, but CD8 T cell mediated effector activity was not seen.
- Thus HIV-1 specific CD8+ cells may be present but may lack direct effector activity in late disease, suggesting that overcoming antigen unresponsiveness may be a useful therapeutic strategy.

HXB2 Location RT (309–317)
Author Location Pol (476–484)

Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords epitope processing, immunodominance
References Sewell *et al.* 1999

- Proteasome regulation influences epitope processing and could influence immunodominance.
- The proteasome is inhibited by lactacystin treatment, and gamma IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome.
- IFN-gamma induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways.
- ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway.
- This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords epitope processing
References Loing *et al.* 2000

- The ILKEPVHGV was modified by the addition of an N-palmitoyl-lysine residue at the P0, P1 or P10 positions of the parent peptide to create a lipopeptide for direct antigen delivery to the cytoplasm for processing.
- The N-terminal modification increased the life span for functional CTL recognition up to 48 hours in comparison to the parent peptide.

HXB2 Location RT (309–317)
Author Location Pol (510–518)
Epitope ILKEPVHGV
Immunogen Vaccine
Vector/Type: canarypox, vaccinia *HIV component:* Env, Gag, Nef, Pol
Species (MHC) human (A*0201)
References Larsson *et al.* 1999

- ELISPOT was used to assay the CD8 T cell response to the HIV-1 proteins Gag, Pol, Nef or Env expressed in vaccinia or canarypox vectors in 19 HIV+ people.
- The highest CTL frequency was directed at epitopes in Pol.
- In A*0201 individuals, higher numbers of spot-forming T cells were directed against HIV-1 proteins expressed in vaccinia than to peptides SLYNTVATL and ILKEPVHGV presented by A2.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords TCR usage
References Wilson *et al.* 1998a

- HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed *in vivo*.
- Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls.
- Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 2/11 of the A2+ individuals responded to ILKEPVHGV, and neither of these two responded to SLYNTVATL.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART
References Gray *et al.* 1999

- Administration of highly active antiretroviral therapy (HAART) reduced CD8+ cell frequency, and the CD8+ cells detected by tetramer staining were likely to be memory cells, indicating that persistently replicating viral populations are needed to maintain high frequencies of HIV-1 specific CTL.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Menendez-Arias *et al.* 1998; Ogg *et al.* 1998b

- HLA-tetrameric complexes were used in a cross-sectional study of 14 untreated HLA A*0201 positive individuals, revealing an inverse relationship between HIV Gag and Pol specific CTL effector cells (CTLe) and viral load.
- Inclusion of both the p17 SLYNTVATL and RT ILKEPVHGV epitopes gives a good representation of HLA A*0201-restricted activity.
- No correlation was observed between the CTLe and CD4 count or clearance rate of productively infected cells.

HXB2 Location RT (309–317)
Author Location RT
Epitope ILKEPVHGV
Immunogen Vaccine
Vector/Type: vaccinia
Species (MHC) human (A*0201)

References Hanke *et al.* 1998a; Hanke *et al.* 1998b
- This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords binding affinity
References Konya *et al.* 1997; Menendez-Arias *et al.* 1998
- This epitope was included as a positive control.
- Binding affinity to A*0201 was measured, $C\_1/2\max\mu M = 12$

HXB2 Location RT (309–317)
Author Location RT (468–476)
Epitope ILKEPVHGV
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
References van der Burg *et al.* 1996
- Immunogenic in humans, slow dissociation rate, and associated with immunogenicity in transgenic HLA-A*0201/K^b mice.
- CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual.

HXB2 Location RT (309–317)
Author Location RT (468–476)
Epitope ILKEPVHGV
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
References van der Burg *et al.* 1995
- Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Menendez-Arias *et al.* 1998; Pogue *et al.* 1995
- Mutational study: position 1 I to Y increases complex stability with HLA-A*0201.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords review, escape
References Goulder *et al.* 1997e; Goulder *et al.* 1997a; Menendez-Arias *et al.* 1998
- HLA-identical sibling hemophiliac brothers were both infected with the same batch of factor VIII.
- One had a response to gag A2 epitope SLYNTVATL, the other to pol A2 epitope ILKEPVHGV. They were tested 6-8 years after infection.
- Viral sequencing from the twin that had no response to SLYNTVATL indicated his virus had the substituted form SLHNAVAVL.
- 71% of an additional set of 22 HIV-1 infected HLA-A*0201 positive donors preferentially responded to gag SLYNTVATL.
- Those individuals with a pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Altman *et al.* 1996
- This paper introduces the tetramer methodology which permits quantification of specific CTL based on expression of specific TCRs—HLA-A2 tetramers were prepared that can stain CTL lines specific for ILKEPVHGV and SLYNTVATL, and can quantify HIV-specific CD8+ cell lines in freshly isolated PBMCs.
- Three patients only stained the Gag epitope SLYNTVATL, one patient had the highest frequency of tetramer staining to the Pol epitope (0.77%), less to the Gag epitope (0.28%)
- The A2-Pol CD8+ clones were CD45RO positive and HLA-DR and CD38 negative, suggesting a memory rather than effector phenotype.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords epitope processing
References Menendez-Arias *et al.* 1998; Walter *et al.* 1997
- HLA-A2 heavy chain and $\beta 2$-microglobulin expressed in E. coli were refolded in the presence of this peptide.
- The HLA-A2-peptide complex elicited HLA-A2 peptide-specific CTL response in cells lacking HLA-A2.
- Suggests that preformed HLA-peptide complexes could provide an alternate to intracellular processing for immunogens.

HXB2 Location RT (309–317)
Author Location RT (464–472)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART
References Gray *et al.* 1999
- Peptide-tetramer complexes of A*0201 and SLYNTVATL or ILKEPVHGV were used to study individuals receiving HAART to determine the frequency of Class I HLA-restricted anti-HIV CD8+ T cells.
- 17/18 asymptomatic patients had a CTL response to one or both epitopes – 72% had a CTL response to SLYNTVATL.
- After HAART, the majority of the epitope-specific CTL were apparently memory cells.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords escape
References Brander *et al.* 1998a

- Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape.
- Only one subject had CTL against all three epitopes.
- Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area.
- C. Brander notes this is an A*0201 epitope.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART
References Ogg *et al.* 1999

- CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SYLVTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient.
- Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy.
- After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days.

HXB2 Location RT (309–317)
Author Location RT (476–484 LAI)
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a A*0201 epitope.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Epitope name IV9
Immunogen HIV-1 infection, in vitro stimulation or selection
Species (MHC) human (A*0201)
References Dela Cruz *et al.* 2000

- Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL.
- These antigens could also be used to stimulate primary responses *in vitro*.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Epitope name P1
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART, escape
References Samri *et al.* 2000

- The epitope was recognized by patient 250#0 but not in another A*0201+ patient, 201#5, in a study of the effects of therapy escape mutations on CTL recognition.

HXB2 Location RT (309–317)
Author Location Pol (LAI)
Epitope ILKEPVHGV
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords dendritic cells
References Engelmayer *et al.* 2001

- Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis through *in vitro* by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors.
- Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific CD4+ helper T-cell responses.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Gea-Banacloche *et al.* 2000

- In a study including many long-term non-progressors, no correlation between plasma virus levels and number of HIV-specific CD8+ T-cells was found.
- High frequencies of circulating CD8+ T-cells were HIV-1 specific, and the majority of these responses were to gag-pol gene products.
- 4/21 subjects were HLA-(A*0201), and of these only 2 subjects (patient 3 and 19) tested positive to this epitope.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords HAART, ART, rate of progression
References Jin *et al.* 2000a

- The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay.
- LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection

Species (MHC) human (A*0201)
References Appay *et al.* 2000

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords dendritic cells
References Ostrowski *et al.* 2000

- The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*
- Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients.
- Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes.
- The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Epitope name RT2
Immunogen Vaccine
Vector/Type: HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT
Species (MHC) human, transgenic mouse (A*0201)
References Guardiola *et al.* 2001

- HLA-A2 transgenic mice were injected with bacteriophage antigens expressing a Th epitope and the HIV CTL epitope ILKEPVHGV, and epitope-specific cytotoxic activity was induced.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords epitope processing, immunodominance
References Sewell *et al.* 2002

- Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing.
- ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Epitope name IL-9
Immunogen HIV-1 infected monocyte-derived
Species (MHC) mouse (A*0201)
References Poluektova *et al.* 2002

- Nonobese diabetic NOD-C.B-17 SCID mice were reconstituted with HLA-A*0201 positive human PBL and injected with HIV-1 infected monocyte-derived macrophages MDM in the basal ganglia to provide a mouse model of HIV-1 encephalitis.
- HLA-A*0201 CTL responses were detected by tetramer staining in the spleen in seven days, increased through day 14, and the numbers of productively infected were reduced >85% in the second week.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Subtype B
Immunogen Vaccine
Vector/Type: peptide *HIV component:* RT *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) transgenic mouse (A*0201)
Keywords binding affinity, vaccine-specific epitope characteristics
References Boissonnas *et al.* 2002

- Ten naturally occurring variants of the Nef epitope VLMWQFDSRL were tested for their affinity to HLA-A*0201 and for their ability to induce gamma-IFN and cytotoxic functions through vaccination of HLA-A*0201 transgenic mice.
- ILKEPVHGV could induce HLA-A*0201 vaccine responses, and was a positive control.

HXB2 Location RT (309–317)
Author Location Pol (468–476)
Epitope ILKEPVHGV
Immunogen Vaccine
Vector/Type: DNA *HIV component:* HIV-1
Species (MHC) mouse (A*0201)
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance
References Singh *et al.* 2002; Sykes & Johnston 1999

- C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome.
- A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members.
- Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV (Pol), RIQRGPGRAFVTIGK (Env) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen.
- The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human, macaque (A*0201)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords epitope processing, dendritic cells
References Andrieu *et al.* 2003

- This study demonstrates that lipopeptides carrying epitopes can be taken up by human dendritic cells, processed using different pathways, and recognized by epitope-specific CD8+ T-cells originally derived from HIV+ individuals. The RT ILKEPVHGV peptide was embedded in a longer peptide fragment in the lipopeptide, and was internalized by endocytosis and processed in the cytosol by proteasomal cleavage by following an endosome-to-cytosol pathway for processing and presentation. Administration of epoxomycin, a proteasome inhibitor, completely abrogated epitope presentation to a CD8+ T-cell line, while monensin, an inhibitor of acid-dependent endosomal enzyme activity did not.
- In contrast to the RT epitope, dendritic cell presentation of the Nef epitope QVPLRPMTYK embedded in a longer peptide in a lipopeptide was not inhibited by epoxomycin, but was inhibited by monensin, indicative of endocytolitic epitope processing.

HXB2 Location RT (309–317)
Author Location
Epitope ILKEPVHGV
Epitope name IV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Assay type cytokine production, proliferation, Tetramer binding, Intracellular cytokine staining, Chromium-release assay
References Dagarag *et al.* 2003

- Telomer length is short in the CD8+ T-cell compartment of HIV-1 infected people, indicating excessive CTL activation and premature senescense. Here human telomerase RT (hTERT) transduction of HIV-1-specific CTL was used to study the functional impact of telomerase. Telomerase expression enhanced proliferative capacity, as well as cytolytic and antiviral capabilities; cytokine production was unchanged. hTERT transduced CTLs were 10-fold more efficient in controlling HIV-1 replication in culture. Thus telomerase transduction can restore CTL mediated cytolysis, and may have therapeutic potential.
- Three polyclonal CD8+ T-cell lines derived from an HIV-1, HLA A*0201 positive patient were used in this study, including one specific for this epitope. An IV9-specific monoclonal cell line, 68A62 was also generated.

HXB2 Location RT (309–317)
Author Location Pol (464–472)
Epitope ILKEPVHGV
Epitope name I9V
Subtype B
Immunogen Vaccine
Vector/Type: peptide *HIV component:* RT *Adjuvant:* CpG immunostimulatory sequence (ISS)
Species (MHC) transgenic mouse (A*0201)
Donor MHC H-A2/Kb
Assay type cytokine production, Tetramer binding, Intracellular cytokine staining, Chromium-release assay
References Daftarian *et al.* 2003

- HLA-A*0201 transgenic mice were immunized with a Th-CTL-fusion peptide composed of the I9V CTL epitope linked to the promiscuous PADRE Th epitope. The peptide only when given in combination with CpG elicited strong I9V-CTL responses.
- The peptide-CpG vaccinated mice, when challenged with pol embedded in vaccinia (pol-vv), could clear the virus from the ovaries. Additionally, intranasal immunized mice given an intranasal pol-vv challenge reduced virus in the lungs.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Epitope name IV9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Assay type Tetramer binding
Keywords genital and mucosal immunity
References Shacklett *et al.* 2003

- Lymphocytes from rectal biopsies were used to characterize the CD8+ T cell response to HIV in GALT, Gut-associated lymphoid tissues. Patients were selected on the basis of being HLA-A2+ and having detectable SLYNTVATL and ILKEPVHGV tetramer responses in PBMC. SLYNTVATL frequency was increased in GALT relative to PBMC in 6/7 patients studied, while a control response to a CMV-peptide was diminished in GALT. Only two patients had ILKEPVHGV CD8+ T cell responses, and both had slightly higher frequencies in GALT than PBMC.
- HIV may perturb lymphocyte retention in GALT, suggested by an overall reduction of GALT CD8+ cells expressing alphaE-beta7. GALT HIV-specific CD8+ T cells expressed alphaE-beta7, suggesting mucosal priming.

HXB2 Location RT (309–317)
Author Location RT (309–317 MN)
Epitope ILKEPVHGV
Subtype B
Immunogen Vaccine
Vector/Type: DNA, polyepitope *Strain:* B clade MN *HIV component:* gp120, Protease, RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) humanized mouse (A*0201)
Assay type CD8 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance, immunotherapy
References Isaguliants *et al.* 2004

- Immunization of HLA-A*0201-transgenic mice with synthetic genes encoding clusters of human A*0201 CTL epitopes located at the sites of drug resistance mutations, induced RT-specific cellular responses indicating the immunogenicity of these constructs. This vaccine strategy may be a first step towards a therapeutic vaccine against drug-resistant strains.
- This was one of five HLA-A*0201 epitopes from the RT or protease proteins that was included in the polyepitope vaccine. When the transgenic HLA A*0202 mice were vaccinated with the polyepitope construct or with a mixture of RT peptides, a sustained low level CD8+ T-cell gamma IFN response was observed, in contrast to when an intact RT gene was used for vaccination.

HXB2 Location RT (309–317)
Author Location
Epitope ILKEPVHGV
Epitope name IV9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, T-cell Elispot, Flow cytometric CTL assay
Keywords epitope processing, escape, kinetics, variant cross-recognition or cross-neutralization
References Jamieson *et al.* 2003

- Epitope escape mutations in chronically infected individuals developed over several years indicating slight selective advantage of escape mutants. The maturation state of CTLs appear to affect the rate of epitope mutation and CTL decay.
- In two patients, IV9 mutations preceded the loss of IV9-specific CD8+ T-cells. In a third patient, escape mutations were coincident with IV9-specific CD8+ T-cell loss. One patient was infected with a ilepvhgA variant, and transiently reverted to the consensus form at year 3. One patient never made a response to IV9 despite being infected with the consensus form of the epitope.

HXB2 Location RT (309–317)
Author Location Gag
Epitope ILKEPVHGV
Epitope name IV9
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Assay type Tetramer binding, Chromium-release assay, Flow cytometric CTL assay
Keywords epitope processing, rate of progression, immunodominance, acute infection, dendritic cells, TCR usage, memory cells
References Kan-Mitchell *et al.* 2004

- In contrast to IV9-CTLs, SL9-CTLs were shown to be primed by immature DCs and independent of help from CD4+ or exogenous IL2 and sensitive to paracrine IL-2 induced apoptosis.

HXB2 Location RT (309–317)
Author Location Pol (468–476 IIIB)
Epitope ILKEPVHGV
Epitope name pol468-476
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* Gag-Pol
Species (MHC) humanized mouse (A*0201)
Assay type Intracellular cytokine staining
Keywords epitope processing, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization, vaccine antigen design
References Singh & Barry 2004

- When A*0201-C3H/J transgenic mice were immunized with plasmids encoding wild-type gag-pol, codon-optimized (CO) gag-pol, and an expression library vaccine expressing 16 fragments of gag-pol fused with ubiquitin for proteosome targeting (ELI), the ELI vaccine produced up to 10-fold higher CD8 T-cell responses than the other two vaccines. In contrast to the wt and CO vaccines, which tended to augment only immunodominant responses, boosting with the ELI vaccine resulted in many CD8 responses against variant epitopes from different HIV-1 clades, and against drug-resistant variants.
- This epitope was recognized in transgenic mice vaccinated with all three vaccine constructs, but the most intense responses were to the ELI vaccine.

HXB2 Location RT (309–317)
Author Location RT (476–484 LAI)
Epitope ILKEPVHGV
Epitope name P1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201, A*0205)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using tetramer staining or CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Immunogen Vaccine
Vector/Type: vaccinia
Species (MHC) human (A2)
References Woodberry *et al.* 1999

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice.
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- ILKEPVHGV was recognized by 2 of the patients.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons, TCR usage
References Kolowos *et al.* 1999

- TCR usage in CTL specific for this epitope was examined in three patients and identical Vβ6.1 and Valpha2.5 gene segments were used and two of the patients had very similar complementarity-determining regions – clonal expansion of RT-HIV-specific CTL can contribute to the skewed TCR repertoire in HIV-1 infected patients.
- CTL clones from all three patients showed similar sensitivity to mutation in the epitope, ilkepvhEv was well recognized (the sequence from SF2), ilkDpvhgv was not (the common A clade form)

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Collins *et al.* 1998

- Nef down-regulates MHC class I molecules, which inhibits CTL killing of HIV-infected targets.
- The anti-RT CTL clone killed Nef- cells less efficiently than anti-gag clones, correlated with the reduced expression of RT.

HXB2 Location RT (309–317)
Author Location RT (476–484 LAI)
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords dendritic cells
References Fan *et al.* 1997

- The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied.

HXB2 Location RT (309–317)
Author Location RT (464–472)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords dendritic cells
References Kundu *et al.* 1998b

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients.
- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated.
- ILKEPVHGV is a conserved HLA-A2 epitope included in this study – 5/6 patients had this sequence as their HIV direct sequence, and these had a detectable CTL response– one person carried the form ILREPVHGV and had no detectable CTL.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Menendez-Arias *et al.* 1998; Tsomides *et al.* 1994

- CTL clones recognize naturally processed peptide – peptide abundance corresponded to level of CTL killing.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A subtype consensus is ILKDPVHGV.
- The D subtype consensus is identical to the epitope ILKEPVHGV.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Cao *et al.* 1997a; Menendez-Arias *et al.* 1998

- The consensus peptides of B and D clade viruses and some As have the sequence ILKEPVHGV.
- The consensus peptide of a subset of A clade viruses, ILKDPVHGV, is not cross-reactive.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Menendez-Arias *et al.* 1998; Yang *et al.* 1996

- CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL.
- Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones.
- The distinction was thought to be due to lower expression of RT relative to Env and Gag.
- CTL can lyse infected cells early after infection, possibly prior to viral production.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CTL suppression of replication
References Yang *et al.* 1997a

- CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*.
- CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation.
- CTL suppress HIV replication more efficiently in HLA-matched cells.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords TCR usage
References Menendez-Arias *et al.* 1998; Moss *et al.* 1995

- Two clones were obtained with different TCR usage, $V_\beta 1$ and $V_\beta 21$.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Menendez-Arias *et al.* 1998; Musey *et al.* 1997

- Cervical CTL clones from an HIV-infected woman recognized this epitope.

HXB2 Location RT (309–317)
Author Location RT (476–484 LAI)
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Menendez-Arias *et al.* 1998; Tsomides *et al.* 1991

- Precise identification of the nonamer that binds to A2.

HXB2 Location RT (309–317)
Author Location RT (476–484 LAI)
Epitope ILKEPVHGV
Subtype B
Immunogen Peptide-HLA interaction
Species (MHC) human (A2)
References Connan *et al.* 1994; Menendez-Arias *et al.* 1998

- Promotes assembly of HLA-A2 molecules in T2 cell lysates.

HXB2 Location RT (309–317)
Author Location RT (510–518)
Epitope ILKEPVHGV
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
References Parker *et al.* 1992

- Studied in the context of HLA-A2 peptide binding.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dyer *et al.* 1999

- CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective.
- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
Keywords dendritic cells
References Zarling *et al.* 1999

- This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses.
- Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA.
- A weak response to KLTPLCVSL was stimulated using macrophages as the APC.
- No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.

HXB2 Location RT (309–317)
Author Location RT (480–)
Epitope ILKEPVHGV
Immunogen computer prediction
Species (MHC) (A2)
Keywords inter-clade comparisons
References Schafer *et al.* 1998

- This study uses EpiMatrix for T cell epitope prediction to identify possible HLA-B27 and A-2 CTL epitopes in HIV.
- Based on EpiMatrix predictions, 28 peptides were synthesized and tested using T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule.
- Two of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV.
- This sequence is not conserved between clades, but is found only in a small number of B clade isolates.

HXB2 Location RT (309–317)
Author Location RT
Epitope ILKEPVHGV
Epitope name RT IV9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- This peptide binds to four HLA-A2 supertype alleles: A*0201, A*0202, A*0206 (highest affinity) and A*6802.
- RT IV9 was recognized in 7/22 patients with chronic HIV-1 infection.
- 1/13 patients with acute HIV-1 infection recognized RT IV9.

HXB2 Location RT (309–317)
Author Location Pol (subtype A)
Epitope ILKDPVHGV
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HIV exposed persistently seronegative (HEPS), escape
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- ILKDPVHGV or ILKEPVHGV was recognized in 1 of the 6 women (ML1760), and the response was present in the last available sample prior to seroconversion, 12 months.
- 20/20 sequences of the infecting strain had no substitutions in this epitope, all were ILKDPVHGV, so there was no evidence for escape.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized by 4/22 HEPS control sex workers: ML887, ML1192, ML1250, and ML1749.

HXB2 Location RT (309–317)
Author Location RT (476–484)
Epitope ILKEPVHGV
Epitope name ILK
Immunogen HIV-1 infection

Species (MHC) human (A2)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- One of the 2/8 HLA-A2+ study subjects recognized this CTL epitope.
- Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQGYFPDWQNY, and GEIYKRWII peptides and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Kostense *et al.* 2001

- HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load.
- Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional.
- In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, immunodominance
References Seth *et al.* 2001

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.
- 6/10 A*0201+ individuals had HIV-specific tetramer staining cells, and 5 of these declined upon successful therapy.
- 3/10 A*0201+ individuals with chronic HIV-1 infection recognized this epitope.
- Prior to therapy, the mean percentage of CD8+ cells that recognized theimmunodominant epitope SLYNTVATL was six-fold greater than the percentage recognizing the epitope ILKEPVHGV.

HXB2 Location RT (309–317)
Author Location RT (476–484 SF2)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 0/6 group 2, and 3/4 group 3.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKDPVHGV
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A2)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- Variants ILK(D/E)PVHGV are A/B clade specific.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-A2 women, 7/10 HEPS and 14/26 HIV-1 infected women recognized this epitope, and ILK(D/E)PVHGV tended to be more reactive in HEPS women, SL(F/Y)NTVATL in infected women.
- The dominant response to this HLA allele was to this epitope in all 7/10 HEPS cases but in only 5 of the 14/26 HIV-1 infected women.
- Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLN(M/T)LN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24.

- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.
- Subject ML 1250 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, which switched to SL(F/Y)NTVATL post-seroconversion.
- Subject ML 1760 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, and gained responses to epitopes A2 SL(F/Y)NTVATL and B27 KRWII(L/M)GLNK post-seroconversion.

HXB2 Location RT (309–317)
Author Location Pol (93TH253 subtype CRF01)
Epitope ILRIPVHGV
Epitope name P464-472
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.

HXB2 Location RT (309–317)
Author Location Pol (93TH253 subtype CRF01)
Epitope ILRIPVHGV
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by two amino acids: ILKEPVHGV.
- This epitope was not conserved in many subtypes, and exact matches were very rare.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

HXB2 Location RT (309–317)
Author Location
Epitope ILKEPVHGV
Epitope name Pol-IV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A02, 9/29 (31%) recognized this epitope.

HXB2 Location RT (309–317)
Author Location Pol (476–484 LAI)
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, epitope processing
References Kelleher *et al.* 2001a

- Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in in an intracellular context.
- RTV did not alter the presentation two RT A2 epitopes processed by distinct pathways: ILKEPVHGV, generated by the constitutive proteasome containing the MB1 beta subunit, and VIYQYMDDL which is dependent on IFNgamma induction of LMP7 which replaces MB1 in the immunoproteasome, and is destroyed by MB1 in the constitutive proteasome.
- RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKDPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002

- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.

- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location RT (309–317)
Author Location RT (476–484 NL43)
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords class I down-regulation by Nef
References Yang *et al.* 2002

- Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed *in vitro* than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL-43 infected cells. The CTL clone 68A62, specific for the class I A2 presented ILKEPVHGV epitope, was one of four used in this study.

HXB2 Location RT (309–317)
Author Location RT (476–484 BRU)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A2
Keywords epitope processing
References Cohen *et al.* 2002

- The antigen presentation of two A2-restricted epitopes was compared, SLYNTVATL (p17) and ILKEPVHGV (RT). HIV-1 infected cells were more sensitive to lysis by SLYNTVATL-specific CTL than by ILKEPVHGV-specific CTL, because of a higher density of SLYNTVATL-A2 resulting from differences in processing.
- Incubation with a T1-cell proteolytic extract showed that by four hours, 25% of a p17 peptide had a C-term Leu-85 and were SLYNTVATL-precursors, while ILKEPVHGV-precursors were far less frequent (6.8%) even with four times more proteolytic extract after 30 hours.
- p17 was preferentially cleaved between Leu85 and Tyr86, while appropriate Val484 and Tyr485 cleavage was minor for RT.
- In a competition experiment, RSLYNTVATL bound TAP 3.7-fold more efficiently than RT peptides.
- No difference in CTL avidity was detected in six patients with HLA-A2-restricted responses to these epitopes.
- No significant difference in HLA-A2 binding of to p17 or RT epitopes was observed.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Epitope name p9
Immunogen Vaccine
Vector/Type: peptide *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (A2)
References De Lucca *et al.* 2002

- BALB/c mice immunized with the p9 peptide, ILKEPVHGV, elicited specific lymphocyte proliferation activity.
- Exposure of lymphocytes from HIV-negative, HLA-A2 positive people to p9-RNA stimulated lymphocyte proliferation activity to p9. Anti-p9 CTL activity in human lymphocytes incubated with RNA extracted from lymphoid organs of p9-vaccinated mice could be more intensely stimulated.
- This murine RNA also mediated RNA-dependent protein kinase (PKR) and NFkappaB activation in the human lymphocytes, which may be driving the enhanced CTL stimulation in the human cells.

HXB2 Location RT (309–317)
Author Location RT
Epitope ILKEPVHGV
Epitope name ILK
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location RT (309–317)
Author Location p51 (476–484)
Epitope ILKEPVHGV
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* Gag, Pol *Adjuvant:* IL-12
Species (MHC) mouse (A2)
Donor MHC H2/Kb
References Kmieciak *et al.* 2001

- Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with either a p17-p24-p51 fusion protein (vG/P-92) or the Gag-Pol precursor protein (vVK1).
- Compared to vVK1, vG/P-92 induced a significant increase in Gag and Pol induced IFNgamma production and CTL responses, and to the epitopes SLYNTVATL and ILKEPVHGV, as determined by Elispot and 51Cr-release assays.

HXB2 Location RT (309–317)
Author Location RT (309–317 NL-43)
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords class I down-regulation by Nef, escape
References Ali *et al.* 2003

- NL43 was passaged in the presence of Nef KEKGGLEGL-specific CTL clones STD11 and KM3, giving rise to rapid selection of escape mutations, including E93G, E93K, K94N+G99R, G95R+G99R, E98K, E98D, G99R, G99E, L100P, and L100I; insertions, deletions, frameshifts and an early stop codon. 34/36

(94%) of sequences carried mutations in the epitope by seven days, 36/36 (100%) by 14 days.
- Several mutations selected by KEKGGLEGL-specific CTL were shown to impair the down regulation of class I MHC by Nef, in particular E93G, E93K, and a truncation mutation at position 51.
- Nef deletion mutants increased 100-fold NL-43 susceptibility to inhibition by CTL specific for epitopes in other proteins, the A2 epitopes ILKEPVHGV in RT and SLYNTVATL in p17 Gag.

HXB2 Location RT (309–317)
Author Location Pol (476–)
Epitope ILKEPVHGV
Epitope name Pol476
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This epitope was one of the previously identified HLA-A2 epitopes studied.
- 9/17 HIV-infected HLA-A2+ people recognized this epitope.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Epitope name RT2
Subtype B
Immunogen Vaccine, in vitro stimulation or selection *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) transgenic mouse (A2)
References Domingo *et al.* 2003

- A virus-like protein scaffold, called E2DISP, derived from pyruvate dehydrogenase multienzyme from Bacillus stearothermophilus has been engineered to display 60 copies of one or more epitopes on a single molecule.
- The E2DISP scaffold displaying pep23 is able to stimulate a Th responses, and peptide RT2, which is a CTL epitope from HIV-1 RT, was able to elicit a CD8+ T cell response *in vitro* and in a vaccinated HLA-A2 transgenic mouse. Thus the E2DISP scaffold allows cell-entry and access to the class I and class II processing pathways.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Tetramer binding, Flow cytometric CTL assay
Keywords responses in children
References Sandberg *et al.* 2003

- 65 vertically HIV-1 infected children, ages 1-16, the majority undergoing ART, were analyzed in regard to their plasma viremia and CD4+ and CD8+ T cell counts, and CD8+ T cell responses.
- Using vaccina expressed Gag, Pol, Env, Rev, Nef in target cells in an Elispot assay, 85% of the children recognized at least one HIV antigen. The strong CD8+ T cell responses were directed against Pol, followed by Gag and Nef. Children younger than 4 had significantly weaker responses (7/14 had no reponse) than older children (only 1/32 had no response, and responses were greater in magnitude).
- SLYNTVATL and ILKEPVHGV tetramers were used to quantitate specific responses. 49 chlidren in an expanded cohort carried HLA-A2. 1/11 children under 3 years of age had detectable CD8+ T-cell responses to SLYNTVATL, 2/11 to ILKEPVHGV. Among children over 3, 11/38 recognized SLYNTVATL and 9/38 recognized ILKEPVHGV.
- Older children that maintained a CD4 count greater than 400 cells/ul tended to have stronger CTL reponses.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) (A2)
Donor MHC A2, A3, B27, B51; A2, A3, B27, B57; A2, A23, B57
Assay type cytokine production, CD8 T-cell Elispot - IFNγ, Tetramer binding, Intracellular cytokine staining
Keywords assay standardization/improvement, memory cells
References Sun *et al.* 2003

- This study compares assay methods for testing CTL responses using samples from 20 HIV+ patients. The study compares ELISpot, tetramer-binding, and intracellular IFNγ. Tetramer-bidning analysis was performed with Gag (SLYNTVATL) or Pol (ILKEPVHGV) tetramers. Antigen presentation using recombinant vaccinia viruses (rVVs) encoding HIV-LAI Gag, Pol, Env, Nef, Tat and Vif proteins was compared to peptide panels. HIV antigen recognition in memory CTLs was measured by chronium release assay and compared to effector/memory CD8+ T cells in an IFN-γ ELISpot assay.
- Results: IFNγ Elispot and flow cytometry gave similar frequencies of HIV specific CD8+ Tcells. Tetramer-binding analysis was most sensitive. Pools of peptides and the sum of frequencies of individual peptides were comparable. Elispot assays using peptides were more sensitive than assays using vaccinia expressed proteins. Cr release and Elispot against rVVs gave comparable memory cell responses 2/3s of the time.
- 3/7 HLA-A2+ patients recognized this epitope.

HXB2 Location RT (309–317)
Author Location RT (309–317 NL43)
Epitope ILKEPVHGV
Epitope name IV9

Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Chromium-release assay, CTL suppression of replication
Keywords escape
References Yang *et al.* 2003a

- Virus was cultured in the presence of CTL lines specific for 4 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts.
- There was one cloned cell line that recognized ILKEPVHGV, 68A62. After 2 weeks of passaging HIV-1 in the presence of 68A62, the mutated epitope ilkeLvhgv was found in 6/12 sequences.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- 2/11 HLA A2+ infection-resistant men, compared to 1/9 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location RT (309–317)
Author Location RT Pol (464–472)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 9/19 patients recognized this epitope.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Epitope name RT-IV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Chromium-release assay
Keywords binding affinity, TCR usage, characterizing CD8+ T cell responses
References Yang *et al.* 2003b

- Killing efficiency of CTLs and their ability to suppress viral replication is shown to depend more on epitope specificity than to antigenic avidity. Different clones recognizing the same epitope had similar killing efficiency despite their variation in avidity. Nef specific CTL clones tended to be most inhibitory, followed by Gag, then by RT specific clones, regardless of avidity.
- 2/14 CTL T-cell clones tested were specific for RT/IV9. Under conditions of excess peptide (100ug/ml), there was no difference in their lytic potential; all possessed similar effector capacity. Avidity was measured as the sensitizing dose of peptide required for 50% of maximal killing (SD50), which varied from 20 pg/ml to 100 ng/ml, over four orders of magnitude for all 14 epitopes. The SD50 values for the two RT/IV9 clones were very different, 50 and 20,000 pg/ml.

HXB2 Location RT (309–317)
Author Location (B consensus)
Epitope ILKEPVHGV
Epitope name IV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A02, A03, B08, B62, Cw7, Cw10
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Chromium-release assay

Keywords assay standardization/improvement
References Lubong *et al.* 2004

- Using IL7 or IL15 in culturing of HIV-1 specific CTL clones was inferior to using IL-2 alone and the addition of these cytokines to IL-2 did not show any advantage. Neither proliferation, survival or lytic capacity of HIV-1-specific CTLs was significantly enhanced by addition of IL7 or IL15.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2)
Donor MHC A02, A30, B4402, B15
Assay type Tetramer binding, T-cell Elispot
Keywords HIV exposed persistently seronegative (HEPS)
References Missale *et al.* 2004

- HIV-specific T-cell response was tested in HIV-uninfected patients exposed to blood from a patient with highly replicating HIV; these same patients were nosocomially infected with HBV. HIV-specific T-cell responses were directed to structural and non-structural HIV proteins in two patients suggesting that the virus replicated in these patients sufficiently to prime a cell-mediated immune response that protected these individuals from HIV infection.
- This patient responded to 4/8 HIV epitopes tested in an IFNgamma EliSpot assay or tetramer assay. Responses were detected 8 and 28 weeks after exposure. A response to ILKEPVHGV was detected by both assays.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country United Kingdom.
Assay type Tetramer binding, T-cell Elispot, Intracellular cytokine staining
Keywords rate of progression, acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Papagno *et al.* 2004

- Acute HIV-1 infection induces massive activation of HIV-specific and non-HIV-specific CD8+ T-cells resulting in differentiation of these cells. High differentiation of CD8+ T-cells is correlated with disease progression. Differentiation is a natural process but it can be driven by elevated immune activation, such as in HIV infection.

HXB2 Location RT (309–317)
Author Location (309–317)
Epitope ILKEPVHGV
Epitope name RT2
Immunogen Vaccine
Vector/Type: bacteriophage coat protein, dihydrolipoyl acetyltransferase E2 protein, of Bacillus stearothermophilus *HIV component:* RT
Species (MHC) transgenic mouse (A2)
Assay type Chromium-release assay
Keywords vaccine antigen design
References De Berardinis *et al.* 2003

- An RT T-helper (KDSWTVNDIQKLVGK) that can be promiscuously presented by multiple HLA-DR molecules, and an RT CTL epitope (ILKEPVHGV) presented by HLA-A2, were displayed using two different antigen presentation systems, bacteriophage virions or E2 protein scaffolds. Both systems enabled display of the epitopes in a mouse model system to the immune system. CTL responses were detected in immunized mice, and were processed correctly for both class I and class II presentation.

HXB2 Location RT (309–317)
Author Location Pol (476–484)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

HXB2 Location RT (309–317)
Author Location Pol (464–472)
Epitope ILKEPVHGV
Immunogen HIV-1 infection
Species (MHC) human (A2, A*0201)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location RT (309–317)
Author Location Pol (subtype B)
Epitope ILKEPVHGV
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2, A*0202)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.

- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among B and D clade viruses.
- Clade A version of the epitope, ILKDPVHGV, was preferentially recognized by CTL.

HXB2 Location RT (309–317)
Author Location RT (309–317)
Epitope ILKEPVHGV
Epitope name RT2
Immunogen Vaccine, in vitro stimulation or selection *Vector/Type:* HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT
Species (MHC) human, mouse (A2, A2 transgenic)
Keywords epitope processing
References De Berardinis *et al.* 2000

- Phage display of the CTL epitope, ILKEPVHGV coupled with T helper epitope KDSWTVNDIQKLVGK, elicited specific CTL responses *in vitro* in PBMC from HIV negative individuals in and *in vivo* in immunization of HLA-A2 transgenic mice.
- Bacteriophage presentation of peptides is generally used for stimulation of antibodies, and this novel discovery of CTL epitope processing and presentation suggests new possibilities for these vectors.

HXB2 Location RT (309–317)
Author Location Pol
Epitope ILKEPVHGV
Immunogen Vaccine *Vector/Type:* DNA
Species (MHC) transgenic mouse (A2.1)
References Ishioka *et al.* 1999

- A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed.
- The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans.
- HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong responses were observed to all nine epitopes, and CTL memory persisted up to four months after a single injection.

HXB2 Location RT (309–317)
Author Location RT (476–484 LAI)
Epitope ILKEPVHGV
Epitope name LR22
Subtype B
Immunogen Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG
Species (MHC) mouse (A2.1)
Keywords binding affinity, vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2001

- The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01).
- The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.
- HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants.
- All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.

HXB2 Location RT (309–317)
Author Location RT (476–484 LAI)
Epitope ILKEPVHGV
Epitope name LR22
Subtype B
Immunogen Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30
Species (MHC) mouse (A2.1)
Keywords vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2002

- When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination Peter *et al.* [2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.

HXB2 Location RT (309–318)
Author Location Pol
Epitope ILKEPVHGVY
Epitope name 1249
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A02, A30, B39,?, ?; A02, A03, B44,?, Cw05, Cw07; A02, A30, B35, B49, Cw04, Cw07
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for ILKEPVHGVY: 96% Promiscuous epitope binding to A02 and Bw62.

HXB2 Location RT (309–318)
Author Location RT (476–485 LAI)
Epitope ILKEPVHGVY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1501)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*1501 epitope.

HXB2 Location RT (309–318)
Author Location RT (309–317)
Epitope ILKEPVHGVY
Immunogen HIV-1 infection
Species (MHC) human (B15)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location RT (309–318)
Author Location RT (309–318)
Epitope IKLEPVHGVY
Immunogen HIV-1 infection
Species (MHC) human (B62)
Keywords immunodominance
References Day *et al.* 2001

- No immunodominant responses were detected to four B62-restricted epitopes tested.

HXB2 Location RT (309–318)
Author Location RT (476–485 LAI)
Epitope ILKEPVHGVY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Bw62)
Keywords review
References McMichael & Walker 1994; Menendez-Arias *et al.* 1998

- Review of HIV CTL epitopes.

HXB2 Location RT (309–318)
Author Location Pol
Epitope ILKEPVHGVY
Subtype A, B, D
Immunogen HIV-1 infection, Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human (Bw62)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location RT (328–352)
Author Location RT (495–515 LAI)
Epitope EIQKQGQGQWTYQIYQEPFKNLKTG
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Menendez-Arias *et al.* 1998; Walker *et al.* 1989

- One of five epitopes defined for RT-specific CTL clones in this study.

HXB2 Location RT (340–350)
Author Location RT (507–516)
Epitope QIYQEPFKNLK
Immunogen HIV-1 infection
Species (MHC) human
References Menendez-Arias *et al.* 1998; Price *et al.* 1995

- Study of cytokines released by HIV-1 specific activated CTL.

HXB2 Location RT (340–350)
Author Location Pol (487–497 93TH253 subtype CRF01)
Epitope QIYQEPFKNLK

Epitope name P495-505
Subtype CRF01_AE
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33.
- This epitope was reactive in HIV+ study subjects 053 and 184 who carried HLA-A11.

HXB2 Location RT (340–350)
Author Location Pol (487–497 93TH253 subtype CRF01)
Epitope QIYQEPFKNLK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This epitope was not predicted by the EpiMatrix method to be likely to bind to A11, though it served as an epitope in the FSWs, and it was one of the six A11 epitopes that had been previously defined.
- 5/8 tested FSWs recognized this epitope.
- This epitope was highly conserved in other subtypes, although exact matches were not very common.

HXB2 Location RT (340–352)
Author Location RT (507–519 LAI)
Epitope QIYQEPFKNLKTG
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords review
References Johnson & Walker 1994; Menendez-Arias *et al.* 1998

- This epitope was listed in a review.

HXB2 Location RT (340–352)
Author Location Pol (495–507)
Epitope QIYQEPFKNLKTG
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location RT (341–349)
Author Location (C consensus)
Epitope IYQEPFKNL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*2301)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location RT (341–350)
Author Location RT (508–516)
Epitope IYQEPFKNLK
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
References Culmann 1998

- C. Brander notes that this is an A*1101 epitope in the 1999 database.

HXB2 Location RT (341–350)
Author Location RT (508–517 LAI)
Epitope IYQEPFKNLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*1101 epitope.

HXB2 Location RT (341–350)
Author Location RT (508–517 SF2)
Epitope IYQEPFKNLK
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.

- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 1/2 group 3.

HXB2 Location RT (341–350)
Author Location Pol (508–516)
Epitope IYQEPFKNLK
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location RT (356–365)
Author Location
Epitope RMRGAHTNDV
Epitope name Pol-RV10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Donor MHC A*2904 A*3002 B*1503 B*5802 Cw*0202 Cw*0602
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subject 01RCH50 also recognized the epitope WRFDSRLAF, Nef(183-191), B*1503.
- Among HIV+ individuals who carried HLA A30, 5/16 (31%) recognized this epitope.

HXB2 Location RT (356–365)
Author Location RT (356–365)
Epitope RMRGAHTNDV
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location RT (356–366)
Author Location RT (356–366)
Epitope RMRGAHTNDVK
Immunogen HIV-1 infection
Species (MHC) human (A*03)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location RT (356–366)
Author Location RT (15–26)
Epitope RMRGAHTNDVK
Epitope name A3-RK11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 5/7 individuals began to have detectable responses to this epitope after STI.

HXB2 Location RT (356–366)
Author Location RT (356–366)
Epitope RTRGAHTNDVK
Epitope name A3-RK11 Pol
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant rtrgahtndvR. The CTL response to both variants declined over time, and the response to the second variant was lower than to the first throughout.

HXB2 Location RT (356–366)
Author Location (B consensus)
Epitope RMRGAHTNDVK
Epitope name RK11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A02, A03, B08, B62, Cw7, Cw10

Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location RT (364–372)
Author Location RT (518–526 U455)
Epitope DVKQLTEVV
Immunogen
Species (MHC) human (A28, A*6802)
Keywords inter-clade comparisons
References Dong 1998; Menendez-Arias *et al.* 1998

- Predicted on binding motif, no truncations analyzed.
- Reacts with clade A consensus (U455), and with the peptide DVKQLAEAV, from the D clade.

HXB2 Location RT (364–372)
Author Location RT (470–478 subtype A)
Epitope DVKQLTEVV
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (B70)
Keywords inter-clade comparisons
References Dorrell *et al.* 1999

- CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa.
- This CTL response was defined in a patient with an A subtype infection.
- Bulk cultures from this patient gave a CTL response that could recognize the subtype D form of this epitope, with two substitutions (DVKQLAEAV), though a CTL line from these cultures didn't recognize the B clade variant (DVKQLTEAV)

HXB2 Location RT (366–385)
Author Location Pol (521–540)
Epitope KQLTEAVOKIAMESIVIWGK
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location RT (373–390)
Author Location RT (373–390 HXB2)
Epitope QKIATESIVIWGKTPKFK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 21% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location RT (374–383)
Author Location RT (LAI)
Epitope KITTESIVIW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords rate of progression
References Menendez-Arias *et al.* 1998; van der Burg *et al.* 1997

- Patients studied were from the Amsterdam cohort.
- CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS); no differences could be found in the degree of conservation between them.
- Epitope recognized by LTS and by a progressor.

HXB2 Location RT (374–383)
Author Location RT (LAI)
Epitope KITTESIVIW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
References van der Burg *et al.* 1997

- Recognized by CTL from a progressor and a long-term survivor, PIVLPEKDSW was also recognized.

HXB2 Location RT (374–383)
Author Location RT Pol (529–538)
Epitope KITTESIVIW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 7 patients recognized this epitope.

HXB2 Location RT (375–383)
Author Location RT (375–383 LAI)
Epitope ITTESIVIW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701, B*5801)
Keywords rate of progression
References Klein *et al.* 1998

- Another patient recognized the ten-mer version of this epitope, KITTESIVIW van der Burg *et al.* [1997]
- B57 has been associated with long-term non-progression in the Amsterdam cohort.
- The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag.
- The patient that recognized ITTESIVIW also recognized IVLPEKDSW.

HXB2 Location RT (375–383)
Author Location RT (375–383)
Epitope IAMESIVIW
Immunogen
Species (MHC) human (B*5801)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location RT (375–383)
Author Location (C consensus)
Epitope IAMESIVIW
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*5801, B*57)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location RT (375–383)
Author Location RT (375–383 SF2)
Epitope ITTESIVIW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with preseroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/2 group 3.

HXB2 Location RT (392–401)
Author Location RT (559–568 LAI)
Epitope PIQKETWETW
Subtype B
Immunogen
Species (MHC) human (A*3201)
References Harrer *et al.* 1996b; Menendez-Arias *et al.* 1998

- Reviewed in Menendez-Arias *et al.* [1998], suggest the epitope is HLA B53/Cw2.
- C. Brander notes that this is an A*3201 epitope in the 1999 database.

HXB2 Location RT (392–401)
Author Location RT (559–568 LAI)
Epitope PIQKETWETW
Subtype B
Immunogen
Species (MHC) human (A*3201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*3201 epitope.

HXB2 Location RT (392–401)
Author Location
Epitope PIQKETWETW
Epitope name Pol-PW10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*3201)
Donor MHC 01RCH59 A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previou.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated.
- Subject 01RCH59 was Hispanic, was not on HAART, viral load 5100, CD4 count 349, and she also recognized QASQEVKNW, p24(176-184), B*5301.
- Among HIV+ individuals who carried HLA A32, 1/2 (50%) recognized this epitope.

HXB2 Location RT (392–401)
Author Location RT (559–568 SF2)
Epitope PIQKETWETW
Immunogen HIV-1 infection
Species (MHC) human (A32)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A32+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/0 group 3.

HXB2 Location RT (392–401)
Author Location RT
Epitope PIQKETWETW
Epitope name A32-PW10(RT)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A32)
Donor MHC A32, A?, B7, B14; A32, A?, B44, B?; A30, A32, B18, B27
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT). Patient B displayed the greatest response to epitope B44-AW11(p24) and also responded to A32-PW10(RT) in both PB and LN samples, while a third response against epitope A32-RW10(gp120) was only detected in the LN sample. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).

HXB2 Location RT (397–406)
Author Location RT (LAI)
Epitope TWETWWTEYW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Menendez-Arias *et al.* 1998; van der Burg *et al.* 1997

- Recognized by CTL from two progressors, EILKEPVGHGV and EELRQHLLRW were also recognized by one, and RETKLGKAGY was also recognized by the other.

HXB2 Location RT (397–406)
Author Location RT Pol (552–561)
Epitope TWETWWTEYW
Immunogen HIV-1 infection
Species (MHC) human (B44)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase

significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 11 patients recognized this epitope.

HXB2 Location RT (407–416)
Author Location (C consensus)
Epitope QATWIPEWEF
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location RT (416–423)
Author Location Pol (571–)
Epitope FVNTPPLV
Epitope name Pol571
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced a CTL responses 1/6 transgenic mice. Responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.

HXB2 Location RT (416–424)
Author Location Pol (563–571 93TH253 subtype CRF01)
Epitope FVNTPPLVK
Epitope name P571-579
Subtype CRF01_AE
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33.

HXB2 Location RT (416–424)
Author Location Pol (563–571 93TH253 subtype CRF01)
Epitope FVNTPPLVK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 1/8 tested FSWs recognized it.
- This epitope was conserved many subtypes (but not subtype H), but exact matches were not very common.

HXB2 Location RT (421–429)
Author Location RT (421–429)
Epitope PLVKLWYQL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules.

HXB2 Location RT (432–440)
Author Location RT (587–597 SF2)
Epitope EPIVGAETF
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords review
References Menendez-Arias *et al.* 1998; Tomiyama *et al.* 1997

- A CTL clone responsive to this epitope was obtained.
- 5/7 B35-positive individuals had a CTL response to this epitope.
- An E to D substitution at position 1, and V to I at position 4, reduces activity but not binding to B*3501.

- Menendez-Arias *et al.* [1998] note in their review that this epitope is near the protease cleavage site and conservation of this region is important for proper viral maturation.

HXB2 Location RT (432–440)
Author Location Pol (587–595)
Epitope EPIVGAETF
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 2000a

- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A.
- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals.
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm.
- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

HXB2 Location RT (432–440)
Author Location
Epitope EPIVGAETF
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location RT (432–440)
Author Location Pol (587–595)
Epitope EPIVGAETF
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Dyer *et al.* 1999

- CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective.
- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.

HXB2 Location RT (432–440)
Author Location Pol
Epitope EPIVGAETF
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- No one, 0/3 HLA B35+ infection-resistant men, and 0/5 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location RT (432–440)
Author Location RT (587–596 SF2)
Epitope EPIVGAETF
Immunogen HIV-1 infection
Species (MHC) human (B35, B51)
References Shiga *et al.* 1996

- Binds HLA-B*3501, and is also presented by B51 – but CTL could not kill RT-vaccinia virus infected cells that expressed B51.

HXB2 Location RT (432–440)
Author Location Pol (587–595)
Epitope EPIVGAETF
Immunogen HIV-1 infection
Species (MHC) human (B35, B51)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location RT (432–440)
Author Location RT (432–440)
Epitope EPIVGAETF
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape

References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location RT (432–441)
Author Location Pol (587–596)
Epitope EPIVGAETFY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 2000a

- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A.
- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals.
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm.
- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

HXB2 Location RT (432–441)
Author Location RT (587–597 SF2)
Epitope EPIVGAETFY
Immunogen HIV-1 infection
Species (MHC) mouse (B35)
Keywords review
References Menendez-Arias *et al.* 1998; Shiga *et al.* 1996

- Binds HLA-B*3501, but not presented by B51, in contrast to the peptide EPIVGAETF.
- Menendez-Arias *et al.* [1998] note in their review that this epitope is located near the protease cleavage site and conservation of this region is important for viral maturation.
- This epitope spans the Pol p66 RT – p15 (RNAse) domain.

HXB2 Location RT (432–441)
Author Location RT (587–597 SF2)
Epitope EPIVGAETFY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords rate of progression
References Kawana *et al.* 1999

- HLA B35 is associated with rapid disease progression.
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals.
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation.

HXB2 Location RT (432–441)
Author Location Pol (587–596)
Epitope EPIVGAETFY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35, B51)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- None of seven patients responded to this peptide with GzB producing cells, while two of the patients responded with IFN-gamma producing cells.

HXB2 Location RT (434–447)
Author Location RT (LAI)
Epitope IVGAETFYVDGAAS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*6802)
References Menendez-Arias *et al.* 1998; van der Burg *et al.* 1997

- Recognized by CTL from a long-term survivor that recognized a set of 5 overlapping peptides spanning IVGAETFYVDGAAS as well as PIVLPEKDSW and KITTESIVIW.
- A*6802 is a subset of HLA-A28.
- This epitope spans the Pol p66 RT – p15 (RNAse) domain.

HXB2 Location RT (436–445)
Author Location RT (591–600 IIIB)
Epitope GAETFYVDGA
Immunogen HIV-1 infection
Species (MHC) human (B45)
References Menendez-Arias *et al.* 1998

- This epitope spans the Pol p66 RT – p15 (RNAse) domain.

HXB2 Location RT (436–445)
Author Location Pol (591–600 IIIB)
Epitope GVETFYVDGA
Immunogen HIV-1 infection
Species (MHC) human (B45)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- No variants of this epitope were found in a non-transmitting mother who had a CTL response to it.
- This epitope spans the Pol p66 RT – p15 (RNAse) domain.

HXB2 Location RT (437–445)
Author Location

Epitope AETFYVDGA
Epitope name Pol-AA9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4501)
Donor MHC A*3002 A*3201 B*4501 B*5301 Cw*0401 Cw*1202
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes YPLTFGWCY, Nef(135-143), HLA B*5301; RSLYNTVATLY, p17(76-86), HLA A*3002; and HIGPGRAFY, gp160(310-318), HLA A*3002.
- Among HIV+ individuals who carried HLA B45, 3/9 (33%) recognized this epitope.

HXB2 Location RT (437–447)
Author Location RT (592–602 LAI)
Epitope AETFYVDGAAN
Subtype B
Immunogen
Species (MHC) human (A28)
References Brander & Walker 1996; Menendez-Arias *et al.* 1998

- P. Johnson, pers. comm.
- This epitope spans the Pol p66 RT – p15 (RNAse) domain.

HXB2 Location RT (437–447)
Author Location Pol (592–602)
Epitope AETFYVDGAAN
Immunogen HIV-1 infection
Species (MHC) human (A28)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location RT (438–448)
Author Location RT (593–603 IIIB)
Epitope ETFYVDGAANR
Immunogen HIV-1 infection
Species (MHC) human (A26)
References Menendez-Arias *et al.* 1998

- This epitope spans the Pol p66 RT – p15 (RNAse) domain.

HXB2 Location RT (438–448)
Author Location Pol (593–603 IIIB)
Epitope ETFYVDGAANR
Immunogen HIV-1 infection
Species (MHC) human (A26)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- One other variant was found that gave a positive, though reduced, CTL response: ETYYVNGAANR.
- This epitope spans the Pol p66 RT – p15 (RNAse) domain.

HXB2 Location RT (440–448)
Author Location Pol (594–602 SF2)
Epitope FYVDGAANR
Subtype B
Immunogen HIV-1 infection, computer prediction
Species (MHC) human (A*3303)
Assay type Chromium-release assay
Keywords binding affinity, computational epitope prediction
References Hossain *et al.* 2003

- HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing.
- This epitope is one of the 4 that are properly processed.

HXB2 Location RT (448–457)
Author Location RT
Epitope RETKLGKAGY
Immunogen HIV-1 infection
Species (MHC) human (A29)
Keywords rate of progression
References van der Burg *et al.* 1997

- Patients studied were from the Amsterdam cohort.
- CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS) and no differences could be found in the degree of conservation between them.
- Epitope recognized by a LTS.
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (449–457)
Author Location
Epitope ETKLGKAGY
Epitope name Pol-EY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2601)
Donor MHC A*3303 A*2601 B*5801 B*8201 Cw*0302 Cw*0701
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.

- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subject 03RCH40 was African American, had a viral load of 2500, CD4 count of 372, was not on HAART, and also recognized the epitope DILDLWIY, Nef(108-115), HLA Cw*0701.
- Among HIV+ individuals who carried HLA A26, 2/8 (25%) recognized this epitope.

HXB2 Location RT (449–457)
Author Location Pol (604–612)
Epitope ETKLGKAGY
Immunogen HIV-1 infection
Species (MHC) human (A*2601)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location RT (451–459)
Author Location Pol (606–)
Epitope KLGKAGYVT
Epitope name Pol606
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was an intermediate A2 binder that did not induce CTL or CD8+ T-cell IFN gamma responses in transgenic mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.

HXB2 Location RT (481–505)
Author Location RT (648–672)
Epitope AIYLALQDSGLEVNIVTDSQYALGI
Immunogen HIV-1 infection
Species (MHC) human
References Menendez-Arias *et al.* 1998; Price *et al.* 1995

- Study of cytokines released by HIV-1 specific activated CTL.
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (481–505)
Author Location RT (648–672 PV22)
Epitope AIYLALQDSGLEVNIVTDSQYALGI
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Kalams *et al.* 1994; Menendez-Arias *et al.* 1998

- A CTL response used to study gene usage in HLA-B14 response.
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (485–493)
Author Location Pol (649–659 BH10, LAI)
Epitope ALQDSGLEV
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is IYLALQDSGLE) has similarity with the epidermal growth factor receptor kinase substrate EPS8, fragment ISAAASDSGVE.

HXB2 Location RT (485–493)
Author Location RT (640–648 HXB2R)
Epitope ALQDSGLEV
Immunogen Vaccine
Strain: B clade HXB2 *HIV component:* RT
Species (MHC) human (A2)
References Brander *et al.* 1995

- Epitope studied in the context of inclusion in a synthetic vaccine.
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (485–493)
Author Location RT (640–648 HXB2R)
Epitope ALQDSGLEV
Immunogen HIV-1 infection
Species (MHC) human (A2.1)
References Brander *et al.* 1995; Brander *et al.* 1996

- This epitope was recognized by PBMC from 3/14 HIV+ asymptomatic patients.
- This epitope was used along with Env CTL epitope TLTSCNTSV and a tetanus toxin T helper epitope for a synthetic vaccine.
- This vaccine failed to induce a CTL response, although a helper response was evident.
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (485–505)
Author Location RT (648–672)
Epitope ALQDSGLEVVTDSQYALGI
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Brander & Walker 1995

- Unpublished, S. Kalams.
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (496–505)
Author Location
Epitope VTDSQYALGI
Epitope name Pol-VI10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1503)

Donor MHC A*3002 A*6801 B*0801 B*1503 Cw*0701 Cw*08(02,05)
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subject 01RCH51 was an African American on HAART, viral load 980, CD4 count 811.
- Among HIV+ individuals who carried HLA B15, 1/17 (6%) recognized this epitope.

HXB2 Location RT (496–505)
Author Location Pol (651–660)
Epitope VTDSQYALGI
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location RT (496–505)
Author Location Pol (subtype B)
Epitope VTDSQYALGI
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B14, B*1402)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among A, B and D clade viruses.

HXB2 Location RT (496–505)
Author Location RT (663–672 IIIB)
Epitope VTDSQYALGI
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
References Brander & Walker 1996

- Unpublished, P. Johnson.
- Published in this database in 1995 as B14, but B14 transfected cells did not present the peptide and it is thought to be presented by the genetically linked Cw8 molecule instead Brander & Walker [1996]
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (496–505)
Author Location RT
Epitope VTDSQYALGI
Immunogen HIV-1 exposed seronegative
Species (MHC) human (Cw8)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A and D subtype consensus are identical to the B clade epitope.
- Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (509–518)
Author Location Pol
Epitope QPDKSESELV
Immunogen
Species (MHC) human (B7)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay.
- QPDKSESELV was newly identified as an HLA-B7 epitope in this study.

HXB2 Location RT (509–518)
Author Location Pol
Epitope QPDKSESELV
Epitope name 1302
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, A24, B07, B38, Cw07, Cw12/13
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for QPDKSESELV: 36%

HXB2 Location RT (516–525)
Author Location RT (516–525)
Epitope ELVNQIIEQL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules.
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (520–528)
Author Location Pol (520–528 LAI)
Epitope QIIEQLIKK
Subtype B
Immunogen
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004; Fukada *et al.* 1999

- C. Brander notes this is an A*1101 epitope.

HXB2 Location RT (520–528)
Author Location Pol (675–683)
Epitope QIIEQLIKK
Subtype B, CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords inter-clade comparisons, TCR usage
References Fukada *et al.* 2002

- Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals.
- QIIEQLIKK was found to elicit clade-specific responses in clade B (QIIEQLIKK is most common) and clade E (qiieElikk is most common). QIIEQLIKK was strongly recognized by CTL from 1/5 B clade infected Japanese subjects, and qiieElikk from 3/7 E clade infected Thai subjects. The variant qiieKliEk, common in the A subtype, was also recognized in 2/7 E clade infected Thai subjects.
- The binding of QIIEQLIKK, qiieElikk and qiieKliEk to HLA A*1101 was similar, but CTL clones from individuals did not cross-react with the cross-clade peptides indicating that the substitutions inhibited TCR interaction.

HXB2 Location RT (520–528)
Author Location RT (80–88)
Epitope QIIEQLIKK
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location RT (520–528)
Author Location Pol
Epitope QIIEQLIKK
Epitope name 1336
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A23, B49, B57, C?
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for QIIEQLIKK: 48%

HXB2 Location RT (530–538)
Author Location Pol (680–691 BH10, LAI)
Epitope KVYLAWVPA
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is IKKEKVYLAWV) has similarity with B-cell growth factor precursor, fragment IKKERLWLGPV.

HXB2 Location RT (530–538)
Author Location
Epitope KVYLAWVPA
Epitope name Pol-KA9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Donor MHC A*0202 A*0301 B*4501 B*5301 Cw*0401 Cw*1502
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- This epitope was newly defined in this study.
- Patient 04RCH86 was Hispanic, not on HAART, and had a viral load of 7600 and CD4 count of i774.
- Among HIV+ individuals who carried HLA A*03, 2/21 (10%) recognized this epitope.

HXB2 Location RT (532–540)
Author Location Pol (687–)
Epitope YLAWVPAHK
Epitope name Pol687
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)

Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was an intermediate A2 binder, and induced a CD8+ T-cell IFN gamma response in 1/6 mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.

HXB2 Location RT (532–540)
Author Location Pol (714–722)
Epitope YLAWVPAHK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location RT (532–540)
Author Location RT (532–540)
Epitope YLAWVPAHK
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Haas *et al.* 1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules.
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.

HXB2 Location RT (532–540)
Author Location RT Pol (687–695)
Epitope YLAWVPAHK
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 3/7 patients recognized this epitope.

II-B-11 RT-Integrase CTL, CD8+, epitopes

HXB2 Location RT-Integrase (560–8)
Author Location Pol (715–723)
Epitope LFLDGIDKA
Immunogen
Species (MHC) human (B*81)
Keywords optimal epitope
References Frahm *et al.* 2004

II-B-12 Integrase CTL, CD8+, epitopes

HXB2 Location Integrase (20–28)
Author Location Pol (762–770)
Epitope RAMASDFNL
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

HXB2 Location Integrase (22–31)
Author Location Pol (764–773)
Epitope MASDFNLPPV
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.

- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)

HXB2 Location Integrase (28–36)
Author Location (C consensus)
Epitope LPPIVAKEI
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*4201)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Integrase (28–36)
Author Location Pol (743–751 SF2)
Epitope LPPVVAKEI
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords inter-clade comparisons, rate of progression
References Tomiyama *et al.* 1999

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed.
- Four of the six epitopes were highly conserved among B subtype sequences – LPPVVAKEI is highly conserved.

HXB2 Location Integrase (28–36)
Author Location Pol (28–36)
Epitope LPPVVAKEI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 7 epitopes from this individual that varied over time, although the internal mutations did not become fixed. The lppIvakei variant arose at intermediate time points.

HXB2 Location Integrase (62–71)
Author Location Pol
Epitope QLDCTHLEGK
Epitope name 1335
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A23, B49, B57, C?; A03, A11, B14, B05, Cw08
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for QLDCTHLEGK: 61%.

HXB2 Location Integrase (82–89)
Author Location RT (797–804 SF2)
Epitope GYIEAEVI
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 1/4 HIV-1 + people tested.
- GYIEAEVI bound to A*2402 weakly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location Integrase (89–98)
Author Location Pol (805–814 BH10, LAI)
Epitope IPAETGQETA
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.

- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is PAETGQETAY) has similarity with Integrin beta-4 precursor (GP150)(CD104), fragment PAETNGEITAY.

HXB2 Location Integrase (89–98)
Author Location Pol
Epitope IPAETGQETA
Immunogen
Species (MHC) human (B56)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay.
- IPAETGQETA was newly identified as an HLA-B56 epitope in this study.

HXB2 Location Integrase (89–98)
Author Location Pol
Epitope IPAETGQETA
Epitope name 1294
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A02, A03, B07, B58, Cw07
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for IPAETGQETA: 8%

HXB2 Location Integrase (96–104)
Author Location Integrase (823–831)
Epitope ETAYFILKL
Immunogen
Species (MHC) human (A*6802)
Keywords inter-clade comparisons
References Dong & Rowland-Jones 1998

- Epitope found in clade A, B, and D – pers. comm. S. Rowland-Jones and T. Dong.

HXB2 Location Integrase (96–104)
Author Location Pol (subtype A)
Epitope ETAYFILKL
Subtype A
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A*6802)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location Integrase (96–104)
Author Location Pol
Epitope ETAYFILKL
Immunogen HIV-1 infection
Species (MHC) human (A*6802)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls (ML1671)

HXB2 Location Integrase (96–104)
Author Location Pol (744–752)
Epitope ETAYFILKL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A*6802)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- ETAYFILKL cross-reacts with clades A, B and D.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-A*6802 women, 3/12 HEPS and 9/11 HIV-1 infected women recognized this epitope likelihood ratio 7.9, p value 0.01, and HEPS women tended to respond to DTVLEDINL, while infected women to ETAYFILKL.
- The dominant response to this HLA allele was to this epitope in 2 of the 3/12 HEPS cases and in all 9/11 HIV-1 infected women that responded to the epitope.

- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.
- Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPG(V/I)RYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.
- Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion.
- Subject ML 1830 made no detectable response prior to seroconversion, but responded to A*6802 DTVLEDINL and A*6802 ETAYFILKL post-seroconversion.

HXB2 Location Integrase (96–104)
Author Location Pol (744–752)
Epitope ETAYFILKL
Immunogen HIV-1 infection
Species (MHC) human (A*6802)
References Appay *et al.* 2000

- This epitope is newly defined in this study.
- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

HXB2 Location Integrase (123–132)
Author Location Integrase (123–132)
Epitope STTVKAACWW
Immunogen
Species (MHC) human (B*57)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Integrase (123–132)
Author Location Integrase
Epitope STTVKAACWW
Epitope name SW10
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords epitope processing, supervised treatment interruptions (STI), rate of progression, immunodominance
References Rodriguez *et al.* 2004

- Protease and Integrase are shown to be frequently targeted by CD8 T-cell responses (23% and 68% of 56 HIV+ patients, respectively). Repsonses tend to cluster in conserved regions of Integrase, although one high conserved region had no responses. CTL frequencies per unit protein length for Protease and Integrase were similar to other HIV non-structural proteins. Three novel, HLA class I-restricted optimal epitopes were found and characterized with fine mapping.
- All five HLA-B57 patients recognized this epitope and were long-term non-progressors.

HXB2 Location Integrase (127–135)
Author Location Pol (869–877)
Epitope KAACWWAGI
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

HXB2 Location Integrase (171–180)
Author Location Pol
Epitope HLKTAVQMAV
Epitope name 1247
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A01, A02, B08, ?, Cw16, ?
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for HLKTAVQMAV: 82%

HXB2 Location Integrase (173–181)
Author Location Pol (888–896)
Epitope KTAVQMAVF
Immunogen
Species (MHC) human (B*5701)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5701 epitope.
- Epitope is motif based, personal communication from C. Hay.
- Subtype of B57 not determined.

HXB2 Location Integrase (173–181)
Author Location Pol (888–896)
Epitope KTAVQMAVF
Immunogen
Species (MHC) human (B57)
References Hay 1999

- Epitope is motif based, personal communication from C. Hay.

HXB2 Location Integrase (177–186)
Author Location Pol (919–928)
Epitope QMAVFIHNFK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location Integrase (178–186)
Author Location Pol (920–928)
Epitope MAVFIHNFK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location Integrase (179–187)
Author Location Pol (921–929)
Epitope AVFIHNFKR
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location Integrase (179–188)
Author Location Integrase (179–188)
Epitope AVFIHNFKRK
Immunogen HIV-1 infection
Species (MHC) human (A*03)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Integrase (179–188)
Author Location Integrase (179–188 LAI)
Epitope AVFIHNFKRK
Subtype B
Immunogen
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004; Fukada *et al.* 1999

- C. Brander notes this is an A*1101 epitope.

HXB2 Location Integrase (179–188)
Author Location Pol (894–903)
Epitope AVFIHNFKRK
Subtype B, CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords inter-clade comparisons
References Fukada *et al.* 2002

- Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals.
- AVFIHNFKRK is commonly found in viruses representing subtypes A-E. It was strongly recognized by CTL from 4/7 E clade infected Thai subjects.

HXB2 Location Integrase (179–188)
Author Location Pol (894–903 93TH253 subtype CRF01)
Epitope AVFIHNFKRK
Epitope name P894-903
Subtype CRF01_AE
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A11)

Keywords HIV exposed persistently seronegative (HEPS)
References Bond *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was weakly reactive in the HEPS study subjects 265 who was HLA A2/A11 and 128 who was HLA A11/A33, and had been predicted to be a possible A11 epitope using Epimer in Bond *et al.* [2001]

HXB2 Location Integrase (179–188)
Author Location Pol
Epitope AVFIHNFKRK
Epitope name 1264
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A11, A3, A68)
Donor MHC A01, A68, B15, B40, Cw03; A03, A11, B14, B51, Cw08, Cw13; A25, A68, B18, B27
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, supertype, computational epitope prediction, immunodominance, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for AVFIHNFKRK:53% Supertype epitope binding to A11, A03 and A68. Immunodominant.

HXB2 Location Integrase (179–188)
Author Location Integrase (894–904)
Epitope AVFIHNFKRK
Epitope name A3-AK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.

HXB2 Location Integrase (179–188)
Author Location Integrase (179–188)
Epitope AVFIHNFKRK
Epitope name A3-AK10 Pol
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant avfVhnfkrk. The CTL response to the second variant was zero at all timepoints. The CTL response to the first variant was low and declined over time.

HXB2 Location Integrase (179–188)
Author Location Pol
Epitope AVFIHNFKRK
Epitope name 1264
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A23, B49, B57, C?; A03, A24, B27, B57, Cw13, Cw18
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for AVFIHNFKRK: 52%

HXB2 Location Integrase (179–196)
Author Location Pol (894–911)
Epitope AVFIHNFKRKGGIGGYSA
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Integrase (185–194)
Author Location Integrase (185–194)
Epitope FKRKGGIGGY
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Integrase (185–194)
Author Location (C consensus)
Epitope FKRKGGIGGY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Integrase (210–227)
Author Location Pol (925–942)
Epitope TKELQKQIIKIQNFRVYY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Integrase (218–235)
Author Location RT-Integrase (218–235 HXB2)
Epitope TKIQNFRVYYRDSRDPLW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 21% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location Integrase (219–227)
Author Location
Epitope KIQNFRVYY
Epitope name Pol-KY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Donor MHC A*0205 A*3002 B*1402 B*5301 Cw*0401 Cw*0802
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Patient 00RCH28 was African American, not on HAART, had a viral load of 5900 and CD4 count of 889, and she also recognized RIRQGLERA, gp160(846-854), A*0205.
- Among HIV+ individuals who carried HLA A30, 6/16 (38%) recognized this epitope.

HXB2 Location Integrase (219–227)
Author Location Integrase (219–227)
Epitope KIQNFRVYY
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Keywords optimal epitope

References Frahm *et al.* 2004

HXB2 Location Integrase (219–227)
Author Location (C consensus)
Epitope KIQNFRVYY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Integrase (219–227)
Author Location Integrase
Epitope KIQNFRVYY
Epitope name KY9
Immunogen HIV-1 infection
Species (MHC) human (A30)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords epitope processing, supervised treatment interruptions (STI), immunodominance
References Rodriguez *et al.* 2004

- Protease and Integrase are shown to be frequently targeted by CD8 T-cell responses (23% and 68% of 56 HIV+ patients, respectively). Repsonses tend to cluster in conserved regions of Integrase, although one high conserved region had no responses. CTL frequencies per unit protein length for Protease and Integrase were similar to other HIV non-structural proteins. Three novel, HLA class I-restricted optimal epitopes were found and characterized with fine mapping.

HXB2 Location Integrase (219–228)
Author Location Pol (934–943 SF2)
Epitope KIQNFRVYYR
Subtype B
Immunogen HIV-1 infection, computer prediction
Species (MHC) human (A*3303)
Assay type Chromium-release assay
Keywords binding affinity, computational epitope prediction
References Hossain *et al.* 2003

- HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing.
- This epitope is one of the 4 that are properly processed.

HXB2 Location Integrase (219–228)
Author Location Pol (919–928)
Epitope KIQNFRVYYR
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location Integrase (241–249)
Author Location Pol (576–584)
Epitope LLWKGEGAV
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
References van der Burg *et al.* 1996

- Slow dissociation rate, associated with immunogenicity in transgenic HLA-A*0201/K^b mice.
- CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual.

HXB2 Location Integrase (241–249)
Author Location Pol (956–964)
Epitope LLWKGEGAV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords dendritic cells
References Kundu *et al.* 1998b

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients.
- 1/6 showed increased Env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated.
- LLWKGEGAV is a conserved HLA-A2 epitope included in this study – 6/6 patients had this sequence as their HIV direct sequence, but only four of these had a detectable CTL response.

HXB2 Location Integrase (241–249)
Author Location Pol (956–964 HXB2R)
Epitope LLWKGEGAV
Immunogen Peptide-HLA interaction
Species (MHC) human (A2)
References Parker *et al.* 1992; Parker *et al.* 1994

- Studied in the context of HLA-A2 peptide binding.

HXB2 Location Integrase (241–249)
Author Location Pol (956–964 HXB2R)
Epitope LLWKGEGAV
Immunogen Peptide-HLA interaction
Species (MHC) human (A2)
References Brander *et al.* 1995

- No CTL activity found in HIV-infected subjects, epitope studied in the context of inclusion in a synthetic vaccine.

HXB2 Location Integrase (241–249)
Author Location Pol (956–964)
Epitope LLWKGEGAW
Immunogen HIV-1 infection
Species (MHC) human (A2, A*0201)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Integrase (241–249)
Author Location RT (956–964 HXB2R)
Epitope LLWKGEGAV
Epitope name LR28
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG
Species (MHC) mouse (A2.1)
Keywords binding affinity, vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2001

- The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01).
- The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.
- HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants.
- All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.

HXB2 Location Integrase (241–249)
Author Location RT (956–964 HXB2R)
Epitope LLWKGEGAV
Epitope name LR28
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30
Species (MHC) mouse (A2.1)
Keywords vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2002

- When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination Peter *et al.* [2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.

HXB2 Location Integrase (260–268)
Author Location Integrase (260–268)
Epitope VPRRKAKII
Immunogen
Species (MHC) human (B*42)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Integrase (263–271)
Author Location Integrase (263–271)
Epitope RKAKIIRDY
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Integrase (263–271)
Author Location Integrase (263–271)
Epitope RKAKIIRDY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Donor MHC A*2301, B*3501, B*1503 (B72), Cw2, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope.

The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location Integrase (263–271)
Author Location (C consensus)
Epitope RKAKIIKDY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

II-B-13 Pol CTL, CD8+, epitopes

HXB2 Location Pol
Author Location RT (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Buseyne *et al.* 1998a

- This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load.

HXB2 Location Pol
Author Location p66 (LAV)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, dendritic cells
References Zheng *et al.* 1999

- Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone.
- Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway.

HXB2 Location Pol
Author Location Pol (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1
References Wasik *et al.* 2000

- HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of beta-chemokines and IL-2 relative to other HIV+ infants.
- No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors.
- CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs.

HXB2 Location Pol
Author Location Pol (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp41, Protease, V3
Species (MHC) human
References Salmon-Ceron *et al.* 1999

- The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36))
- Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36.
- Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160.

HXB2 Location Pol
Author Location Pol (172–219 subtype B)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade LAI, B clade SF2 *HIV component:* Env, Gag, Nef, Protease
Species (MHC) human
References Gorse *et al.* 1999b

- The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120.

- In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients.
- The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity.

HXB2 Location Pol
Author Location Pol (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Betts *et al.* 1999

- This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection.

HXB2 Location Pol
Author Location Pol (BRU)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Aladdin *et al.* 1999

- In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death.

HXB2 Location Pol
Author Location RT (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Buseyne *et al.* 1998b

- In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes.

HXB2 Location Pol
Author Location RT
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12
Species (MHC) mouse
References Kim *et al.* 1997c

- A gag/pol, vif or gp160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice.
- When IL-12 was present, CTL response could be detected even without *in vitro* stimulation.

HXB2 Location Pol
Author Location RT
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Trickett *et al.* 1998

- Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection.
- Improvement in CD4+ and CD8+ T cells were seen in 7/12, and an increase in the CTL response to Pol was seen in one patient.

HXB2 Location Pol
Author Location RT
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Froebel *et al.* 1997

- Two HIV-1 infected children with contrasting disease courses were followed longitudinally – one died of AIDS, the other is a long-term non-progressor.
- Reactivity against Gag, Pol, Env and Tat proteins was tested by PBMC bulk cultured cells reacting with protein expressed in vaccinia constructs in autologous EBV transformed B cells.
- The child who progressed consistently had CTL against Pol and Tat.
- The long-term non-progressing child had no detectable CTL, but was heterozygous for a mutation in the CCR5 receptor and for HLA-B49, which has been shown to be associated with slower progression.

HXB2 Location Pol
Author Location Pol (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Betts *et al.* 1997

- 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins.
- A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients.

HXB2 Location Pol
Author Location RT
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References De Maria *et al.* 1997

- CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function.
- Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels.

HXB2 Location Pol
Author Location Pol (LAI, MN)

Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human
References Goh *et al.* 1999

- 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype.
- In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins.

HXB2 Location Pol
Author Location Pol (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: canarypox *HIV component:* Gag, gp120, gp41, Nef, Protease, RT
Species (MHC) human
References Evans *et al.* 1999

- A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination.

HXB2 Location Pol
Author Location Gag/Pol (MN)
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86
Species (MHC) chimpanzee
References Kim *et al.* 1998

- The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.

HXB2 Location Pol
Author Location Pol (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Jin *et al.* 1998a

- CTL precursor frequencies were determined in HIV-1 infected pregnant women, and significantly higher CTLp frequencies to Pol and Nef were found in non-transmitting mothers than in transmitting mothers;

HXB2 Location Pol
Author Location Pol
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Young *et al.* 2001

- Addition of recombinant rec human IL12 (rhIL12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/ul > 500.
- 2/10 individuals with <200 CD4 cells/ul, and 3/10 individuals with 200-500 CD4cells/ul, had an increase of >5% upon treatment of the culture with rhIL12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL12.

HXB2 Location Pol
Author Location RT (subtype A, B, D)
Epitope
Subtype A, B, D
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Cao *et al.* 2000

- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D.
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.

HXB2 Location Pol
Author Location Pol
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References White *et al.* 2001

- HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women.

HXB2 Location Pol
Author Location Pol (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Jin *et al.* 2000a

- The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets.
- LTNPs have high memory CTL numbers and low viral load.

HXB2 Location Pol
Author Location Pol
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human

Keywords review, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 2001

- This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population.
- The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays.
- CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases.
- CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response.
- HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people.

HXB2 Location Pol
Author Location
Epitope
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References De Maria *et al.* 1994; Kuhn *et al.* 2002

- 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Pol
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission, rate of progression
References Kuhn *et al.* 2002; Wasik *et al.* 1999

- In HIV-infected infants HIV-specific, CTL responses were not detectable in icord blood or in PBMC collected shortly after birth and were absent or remained very low in 3 infants with a rapidly progressive disease. For those who progressed more slowly, the HIV-specific CTL activity varied.
- The two infants with high levels of Env peptide-stimulated IL-2 responses had the highest CTLp frequencies.
- Stronger responses were detected after initiation of the antiretroviral therapy.
- Two babies that were not infected though born to HIV+ mothers had detectable though low HIV-specific CTLp responses to Env (1/2), Pol (2/2), Gag (1/2) cord blood and transiently in PBMC after birth.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Pol
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References Aldhous *et al.* 1994; Kuhn *et al.* 2002

- Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points.
- Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses Tat (1/2), Pol (2/2), Gag (1/2).
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Pol
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed, however, epitopes were not found that span the invariant, most highly conserved regions of RT and Protease. This might be due to the virus evolving conserved features that disallow the CTL responses in these most conserved regions, as functional constraints for enzyme function would not tolerate change and normal capacity for immune escape by rapid evolution is lost in these domains.

HXB2 Location Pol
Author Location
Epitope
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, inter-clade comparisons
References Loemba *et al.* 2002

- Therapeutic RT inhibitors were used to select *in vitro* for resistance mutations in subtype C viruses. Many of the resistance mutations were located within analogs to CTL epitopes that had been defined for the B subtype,

HXB2 Location Pol
Author Location (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, acute infection
References Ortiz *et al.* 2002

- Subjects treated with HAART early in HIV-infection showed a correlation between the number of viremic episodes and the total as well as the Pol-specific CD8 T-cell activity as measured by Elispot SFC per million PBMC summed across Pol, Env, Nef and Gag. The subjects treated early after infection had higher levels of CD8+ T-cell activity (N = 31) than those treated later (N = 23), and a greater capacity to enhance CD8+ T-cell responses to viremic episodes.

HXB2 Location Pol
Author Location (MN)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Edwards *et al.* 2002

- 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag.
- Nef and/or Pol CTL responses were detected in 86% of the subjects.
- The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load.
- Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count.
- Nef and Env responses did not correlate with either CD4 counts or viral load.

HXB2 Location Pol
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, dendritic cells
References Larsson *et al.* 2002b

- Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.

HXB2 Location Pol
Author Location (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunotherapy
References Trickett *et al.* 2002

- Conditions were optimized for ex-vivo expansion of CD8+ and CD4+ T-cells with the goal of functional T-cell production for autologous immunotherapy. 10,000-fold expansions were obtained in 14 days with optimized concentrations of IL-2, anti-CD3 and anti-CD28 coated microspheres, and decreasing amounts of serum over the first 8 days.

HXB2 Location Pol
Author Location (IIIB)
Epitope
Subtype B
Immunogen HIV-1 and HCV co-infection
Species (MHC) human
Keywords rate of progression
References Lauer *et al.* 2002

- HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins.
- All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load.
- Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted.
- HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.

HXB2 Location Pol
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, responses in children
References Scott *et al.* 2001

- CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age.
- Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses.
- One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol.
- Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.

HXB2 Location Pol

Author Location (IIIB, MN)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords dendritic cells
References Larsson *et al.* 2002a

- Dendritic cells acquire and present HIV-1 antigens derived from dead, apoptotic cells or from non-infectious, fusion-competent HIV-1 virions, and these DC cells could stimulate CD4+ and CD8+ T-cells resulting in IFNgamma production in an Elispot assay. Both HLA Class I and class II molecules were used for presentation. This may be an important aspect of the initial immune response to HIV-1 infection of CD4+ cells in the mucosal subepithelia.

HXB2 Location Pol
Author Location (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, supervised treatment interruptions (STI)
References Ortiz *et al.* 2001

- Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.

HXB2 Location Pol
Author Location
Epitope
Immunogen computer prediction
Species (MHC) (A*0201, B*3501)
Keywords inter-clade comparisons, computational epitope prediction
References Schönbach *et al.* 2002

- Computational methods (artificial neural networks, hidden Markov models, binding matrices based on HLA association rates) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.

HXB2 Location Pol
Author Location Pol
Epitope
Immunogen HIV-1 infection
Species (MHC) human (A*0201, Cw*08)
References Shacklett *et al.* 2000

- HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples.

HXB2 Location Pol
Author Location RT (IIIB)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords epitope processing, escape
References Moore *et al.* 2002b

- HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing.
- 25 negative associations were also found between polymorphism and HLA alleles. The authors propose this is due to escape mutations in epitopes presented by common HLA types dominating in the population, and give examples of five amino acids which are in the consensus and tend to be stable in those with the most common HLA allele, HLA-A2.

HXB2 Location Pol
Author Location Pol
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*35)
Keywords rate of progression
References Jin *et al.* 2002

- Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501.
- Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env.
- The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.

HXB2 Location Pol
Author Location Pol
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade HXB2, B clade NL43 *HIV component:* Gag, Pol

Species (MHC) mouse (H-2^d)
References Huang *et al.* 2001

- Different HIV strains were used for different regions: gag HXB2, pol NL43
- Mice were immunized with four humanized DNA constructs: GagPol, that would form a pseudoparticle carrying Gag and Pol, Gag, Pol or a GagPol fusion construct.
- The GagPol pseudoparticle, Gag and GagPol fusion construct all elicited strong anti-Gag CTL, but only the GagPol fusion construct elicited strong anti -Pol CTL.

II-B-14 Vif CTL, CD8+, epitopes

HXB2 Location Vif (17–26)
Author Location
Epitope RIRTWKSLVK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Vif (17–26)
Author Location Vif (17–26 SF2)
Epitope RIRTWKSLVK
Epitope name RK10
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
References Altfeld *et al.* 2001a

- CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- 10/29 (35%) individuals tested responded to Vif.
- This epitope was recognized by 3/15 individuals expressing A*0301 allele.
- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- Overlapping Vif peptides QVDRMRIRTWKSLVK and RIRTWKSLVKHHMYI both reacted with T-cells from AC-06 and contained epitope RIRTWKSLVK.

HXB2 Location Vif (17–26)
Author Location Vif (17–26)
Epitope RIRTWKSLVK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vif (17–26)
Author Location (LAI)
Epitope RIRTWKSLVK
Subtype B
Immunogen
Species (MHC) (A3)
Keywords optimal epitope
References Altfeld 2000; Frahm *et al.* 2004

HXB2 Location Vif (17–26)
Author Location
Epitope RIRTWKSLVK
Epitope name Vif-RK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A03, 3/21 (14%) recognized this epitope.

HXB2 Location Vif (17–26)
Author Location Vif (17–26)
Epitope RIRTWKSLVK
Epitope name A3-RK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.

- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals had detectable responses to this epitope after STI.

HXB2 Location Vif (17–26)
Author Location Vif (17–26)
Epitope RIRTWKSLVK
Epitope name A3-RK10 Vif
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant riStwkslvk. The initial CTL response to persisted to against both variants after the superinfection was established.

HXB2 Location Vif (17–26)
Author Location Vif (17–26)
Epitope RIRTWKSLVK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location Vif (17–26)
Author Location (B consensus)
Epitope RIRTWKSLVK
Epitope name RK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A02, A03, B08, B62, Cw7, Cw10; A03, B07, Cw7
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow -cytometric cytotoxicity assay based on caspase 3 activation in dying cells, it was shown that a subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exibited stronger intracellular perforine expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforine expression was found.
- 2/9 individuals recognized this epitope, presented by HLA-A3.

HXB2 Location Vif (23–31)
Author Location Vif (23–)
Epitope SLVKHHMYV
Epitope name Vif23(9V)
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Vif *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced CTL and CD8+ T-cell IFN gamma responses in mice. Response was detected in 1/17 HIV+ HLA-A2 subjects.
- The variant slvkhhmyI was an intermediate A2 binder, and stimulated immune reponses in fewer A2 transgenic mice. The same person recognized both variants.

HXB2 Location Vif (27–41)
Author Location Vif
Epitope HHMYISKKAKGWGWFYR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 33% (23/70) targeted one or more Vif peptides, and this peptide was the most frequently recognized epitope in Vif (25%).
- The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.

HXB2 Location Vif (28–36)
Author Location Vif (28–36)
Epitope HMYISKKAK
Immunogen HIV-1 infection
Species (MHC) human (A*03)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vif (28–36)
Author Location Vif (28–36)
Epitope HMYISKKAK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vif (28–36)
Author Location Vif (28–36)
Epitope HMYISKKAK
Epitope name A3-HK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 2/7 individuals had detectable responses to this epitope after STI.

HXB2 Location Vif (31–39)
Author Location
Epitope ISKKAKGWF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Vif (31–39)
Author Location Vif (31–39 SF2)
Epitope ISKKAKGWF
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
References Altfeld *et al.* 2001a

- CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- 10/29 (35%) individuals tested responded to Vif.
- This epitope was recognized by 2/6 individuals expressing B*5701 allele.

HXB2 Location Vif (31–39)
Author Location Vif (31–39)
Epitope ISKKAKGWF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vif (31–39)
Author Location Vif (31–39)
Epitope ISKKAKGWF
Immunogen
Species (MHC) human (B*5701)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vif (48–57)
Author Location
Epitope HPRVSSEVHI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Vif (48–57)
Author Location Vif (48–57 SF2)
Epitope HPRVSSEVHI
Epitope name HI10
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
References Altfeld *et al.* 2001a

- CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- 10/29 (35%) individuals tested responded to Vif.
- This epitope was recognized by 3/8 individuals expressing B*0702 allele.
- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- Overlapping Vif peptides HHYESTHPRVSSEVH and TH-PRVSSEVHIPLG both reacted with T-cells from AC-06 and contained epitope HPRVSSEVHI.

HXB2 Location Vif (48–57)
Author Location Vif (48–57)
Epitope HPRVSSEVHI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vif (48–57)
Author Location Vif (48–57)
Epitope HPRVSSEVHI
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vif (48–57)
Author Location (C consensus)
Epitope HPKVSSEVHI
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*4201)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Vif (48–57)

Author Location Vif (48–57)
Epitope HPRVSSEVHI
Epitope name B7-HI10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.

HXB2 Location Vif (48–57)
Author Location Vif (48–57)
Epitope HPRISSEVHI
Epitope name B7-HM0 Vif
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant hpKissevhi. The CTL response was equal against both variants, and declined over time.

HXB2 Location Vif (48–57)
Author Location (B consensus)
Epitope HPRISSEVHI
Epitope name HI10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, B07, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location Vif (48–57)
Author Location (B consensus)
Epitope HPKISSEVHI
Epitope name HKI10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, B07, Cw7
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location Vif (57–66)
Author Location Vif (57–66)
Epitope IPLGDAKLII
Immunogen
Species (MHC) human (B*51)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vif (61–80)
Author Location Vif (61–80)
Epitope EARLVIKTYWGLOTGERDWH
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Vif (71–90)
Author Location Vif (71–90)

Epitope GLQTGERDWHLGHGVSIEWR
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Vif (79–87)
Author Location Vif (79–87)
Epitope WHLGHVSI
Immunogen HIV-1 infection
Species (MHC) human (B*1510)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vif (79–87)
Author Location Nef (C consensus)
Epitope WHLGHGVSI
Epitope name WI9
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1510)
Donor MHC A*2601, A*7401, B*0801, B*1510, Cw*0202, Cw*0801
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This epitope was one of two used to illustrate how specific epitopes were characterized with regard to defining the optimal epitope and the HLA restricting element. HLA allelic associations in the population with peptide recognition was generally high predictive of the epitope within the 15 mer.

HXB2 Location Vif (79–87)
Author Location (C consensus)
Epitope WHLGHGVSI
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1510)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Vif (79–87)
Author Location Vif (79–87)
Epitope WHLGQGVSI
Immunogen HIV-1 infection
Species (MHC) human (B*3801)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vif (101–109)
Author Location Vif (101–)
Epitope GLADQLIHL
Epitope name Vif101(9L)
Immunogen HIV-1 infection, Vaccine, computer prediction
Vector/Type: peptide *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 3/17 HIV+ HLA-A2 subjects.
- The variant gladqlihM was an intermediate A2 binder, but still could stimulate a response in HLA-A2 transgenic mice. It was not recognized by the 3 people who recognized with GLADQLIHL.

HXB2 Location Vif (101–110)
Author Location Vif
Epitope DLADQLIHLY
Epitope name 1237
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A02, A30, B39,?, ?; A01, A02, B08, ?, Cw16, ?
Assay type T-cell Elispot

Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for DLADQLIHLY: 54%

HXB2 Location Vif (102–111)
Author Location
Epitope LADQLIHLHY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Vif (102–111)
Author Location Vif (102–111 SF2)
Epitope LADQLIHLHY
Immunogen HIV-1 infection
Species (MHC) human (B*1801)
References Altfeld *et al.* 2001a

- CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- 10/29 (35%) individuals tested responded to Vif.
- This epitope was recognized by 2/5 individuals expressing B*1801 allele.

HXB2 Location Vif (102–111)
Author Location Vif (102–111)
Epitope LADQLIHLHY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1801)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vif (102–111)
Author Location Vif (102–111)
Epitope LADQLIHLHY
Immunogen HIV-1 infection
Species (MHC) human (B*1801)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vif (127–135)
Author Location Vif (125–135)
Epitope HIVSPRCEY
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*0201, A29, B58, B62, Cw*0301, Cw*1601
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location Vif (149–157)
Author Location Vif (149–)
Epitope ALAALITPK
Epitope name Vif149
Immunogen HIV-1 infection, Vaccine

Vector/Type: peptide *HIV component:* Vif *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.

HXB2 Location Vif (158–166)
Author Location Vif (158–)
Epitope KIKPPLPSV
Epitope name Vif158(2I)
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Vif *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.
- The substitution kTkpplpsv was also a good binder, but did not elicit a response in transgenic mice, and no reponse to this variant was detected among the 17 HIV+ people tested.

HXB2 Location Vif (158–168)
Author Location Vif (158–168)
Epitope KTKPPLPSVKK
Immunogen HIV-1 infection
Species (MHC) human (A*03)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vif (158–168)
Author Location Vif (158–168)
Epitope KTKPPLPSVKK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vif (158–168)
Author Location (B consensus)
Epitope KTKPPLPSVKK
Epitope name KK11
Immunogen HIV-1 infection
Species (MHC) human (A11)
Donor MHC A02, A11, B18, B44, Cw5, Cw12
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location Vif (158–168)
Author Location Vif (158–168)
Epitope KTKPPLPSVKK
Epitope name A3-KK11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 2/7 individuals had detectable responses to this epitope after STI.

HXB2 Location Vif (158–168)

Author Location Vif (158–168)
Epitope RRKPPLPSIAK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response to 25 distinct epitopes, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant rTkpplpsVTk. The patient maintained persistent reactive CTL against both variants after the superinfection was established.

HXB2 Location Vif (160–169)
Author Location Vif
Epitope KPPLPSVKKL
Immunogen
Species (MHC) human (B7)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay.
- KPPLPSVKKL was newly identified as an HLA-B7 epitope in this study.

HXB2 Location Vif (160–169)
Author Location Vif
Epitope KPPLPSVKKL
Epitope name 1296
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, A24, B07, B38, Cw07, Cw12/13
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for KPPLPSVKKL: 23%

HXB2 Location Vif (168–176)
Author Location Vif
Epitope KLTEDRWNK
Epitope name 1344
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A24, B27, B57, Cw13, Cw18
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for KLTEDRWNK: 54%

HXB2 Location Vif
Author Location Vif
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12
Species (MHC) mouse
References Kim *et al.* 1997c

- A gag/pol, vif or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice.
- When IL-12 was present, CTL response could be detected even without *in vitro* stimulation.

HXB2 Location Vif
Author Location Vif
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Vif, Vpu
Species (MHC) mouse (H-2^d)
Keywords inter-clade comparisons, Th1
References Ayyavoo *et al.* 2000

- Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels.
- Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response.
- IL-4 production was not significantly changed after antigen stimulation compared to control levels.
- Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization-stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.

HXB2 Location Vif
Author Location Vif
Epitope
Immunogen Vaccine

Vector/Type: DNA *HIV component:* Nef, Vif, Vpu
Species (MHC) mouse (H-2^d)
Keywords inter-clade comparisons, Th1
References Ayyavoo *et al.* 2000

- Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels.
- Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response.
- IL-4 production was not significantly changed after antigen stimulation compared to control levels.
- Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization-stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.

II-B-15 Vpr CTL, CD8+, epitopes

HXB2 Location Vpr (12–20)
Author Location
Epitope REPHNEWTL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Vpr (12–20)
Author Location Vpr (12–20 SF2)
Epitope REPHNEWTL
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Keywords acute infection
References Altfeld *et al.* 2001a

- CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection.
- Only one B*4002+ individual was tested, and had a CTL response against REPHNEWTL.
- Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells.

HXB2 Location Vpr (12–20)
Author Location Vpr (12–20)
Epitope REPHNEWTL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vpr (25–40)
Author Location Vpr (25–40 HXB2)
Epitope ELKNEAVRHFPRIWLH
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.

- Responses to this peptide were detected in 17% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location Vpr (29–37)
Author Location Vpr (29–37)
Epitope EAVRHFPRI
Immunogen
Species (MHC) human (B*51)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vpr (29–37)
Author Location Vpr (29–37 B)
Epitope EAVRHFPRI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A*0201, A*2501, B18, B51, Cw*0102, Cw*1203
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location Vpr (30–38)
Author Location
Epitope AVRHFRPIW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Vpr (30–38)
Author Location Vpr (29–38 SF2)
Epitope AVRHFPRIW
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords acute infection
References Altfeld *et al.* 2001a

- CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- This epitope was recognized by 4/6 individuals expressing B*5701 allele.
- Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection.
- Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells.

HXB2 Location Vpr (30–38)
Author Location Vpr (29–38)
Epitope AVRHFPRIW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vpr (30–38)
Author Location Vpr (30–38)
Epitope AVRHFPRIW
Immunogen

Species (MHC) human (B*5701)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vpr (30–38)
Author Location
Epitope AVRHFPRIW
Epitope name Vpr-AW9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B57, 1/7 (14%) recognized this epitope.

HXB2 Location Vpr (31–39)
Author Location Vpr (31–39)
Epitope VRHFPRIWL
Immunogen HIV-1 infection
Species (MHC) human (B*27)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vpr (31–50)
Author Location Vpr (31–50)
Epitope VRHFPRPWLHSLGQYIYETY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Vpr (34–42)
Author Location
Epitope FPRIWLHGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Vpr (34–42)
Author Location Vpr (34–)
Epitope FPRPWLHGL
Epitope name Vpr34
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Vpr *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced a CD8+ T-cell IFN gamma response in 1/6 mice. Responses were detected in 3/17 HIV+ HLA-A2 subjects.

HXB2 Location Vpr (34–42)
Author Location Vpr (34–42 SF2)
Epitope FPRIWLHGL
Epitope name FL9
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords acute infection
References Altfeld *et al.* 2001a

- CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- This epitope was recognized by 2/2 individuals expressing B*8101 allele and 4/8 individuals expressing B*0702 allele.
- Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection.
- Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells.
- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.

- FPRIWLHGL was the only epitope identified in Vpr for AC-06.

HXB2 Location Vpr (34–42)
Author Location Vpr (34–42)
Epitope FPRIWLHGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vpr (34–42)
Author Location Vpr (34–42)
Epitope FPRIWLHGL
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vpr (34–42)
Author Location Vpr (34–42 SF2)
Epitope FPRIWLHGL
Epitope name FL9
Immunogen HIV-1 infection
Species (MHC) human (B*8101)
Keywords acute infection
References Altfeld *et al.* 2001a

- CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- This epitope was recognized by 2/2 individuals expressing B*8101 allele and 4/8 individuals expressing B*0702 allele.
- Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection.
- Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells.

HXB2 Location Vpr (34–42)
Author Location Vpr (34–42)
Epitope FPRIWLHGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*8101)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vpr (34–42)
Author Location Vpr (34–42)
Epitope FPRIWLHGL
Immunogen
Species (MHC) human (B*8101)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vpr (34–42)
Author Location (C consensus)
Epitope FPRPWLHGL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*8101, B*4201, B*0702)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Vpr (34–42)
Author Location Vpr (34–42)
Epitope FPRIWLHGL
Epitope name B7-FL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.

- 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.

HXB2 Location Vpr (34–42)
Author Location Vpr (34–42)
Epitope FPRTWLHGL
Epitope name B7-FL9 Vpr
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.
- The second infecting strain had the variant fpWtwlhgl. The CTL response declined over time and the response to the second variant was lower than to the first one all the time points.

HXB2 Location Vpr (41–49)
Author Location Vpr
Epitope SLGQHIYET
Epitope name Vpr41
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* anchored gp120, Vpr *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type T-cell Elispot, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.

HXB2 Location Vpr (52–62)
Author Location Vpr (52–62)
Epitope DTWAGVEAIIR
Immunogen HIV-1 infection
Species (MHC) human (A*6801)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vpr (53–63)
Author Location Vpr (53–63)
Epitope TWAVEAIIRI
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A1, A3, B7, B14, Cw*0702, Cw*0802
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location Vpr (55–70)
Author Location Vpr
Epitope AGVEAIIRILQQLLFI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 40% (28/70) targeted one or more Vpr peptides, and this peptide was the most frequently recognized epitope in Vpr (41%).
- The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.

HXB2 Location Vpr (59–67)
Author Location
Epitope AIIRILQQL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Vpr (59–67)
Author Location Vpr (58–66 LAI)
Epitope AIIRILQQL
Subtype B
Immunogen
Species (MHC) human (A*0201)
Keywords optimal epitope
References Altfeld *et al.* 2001c; Frahm *et al.* 2004

- C. Brander notes this is an A*0201 epitope.

HXB2 Location Vpr (59–67)
Author Location Vpr (58–66 SF2)
Epitope AIIRILQQL
Epitope name AL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords acute infection
References Altfeld *et al.* 2001a

- CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.
- This epitope was recognized by 8/24 individuals expressing A*0201 allele.
- Epitope is located within a highly conserved alpha helix in Vpr.
- Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection.
- Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells.
- The A2 epitopes Vpr AIIRLLQQL and p17 SLYNTVATL do not account for the dominance of Vpr and p17, the result holds even when HLA-A2+ individuals are excluded.

HXB2 Location Vpr (59–67)
Author Location Vpr (59–)
Epitope AIIRILQQL
Epitope name Vpr-59
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction, immunodominance
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- AIIRILQQL binds to four HLA-A2 supertype alleles: A*0203, A*0201, A*0206 and A*6802 (highest affinity), but not A*0202.
- 5/22 individuals with chronic HIV-1 infection recognized this epitope, but with low magnitude responses in ELISPOT.
- 2/12 HLA-A2 patients with acute HIV-1 infection responded strongly to this peptide, but during chronic infection SL9 and Gag-386 tended to be immunodominant while Vpr-59 was weak and sub-dominant.
- One of the the acutely infected individuals, AC13, was HLA A*0201/68 B44/14 and also had a strong acute response to gp41 epitope SV10 SLLNATDIAV.
- This peptide was shown to be properly processed and presented in TAP-competent B-cell lines *in vitro*.

HXB2 Location Vpr (59–67)
Author Location Vpr (58–66)
Epitope AIIRILQQL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vpr (59–67)
Author Location Vpr (59–67)
Epitope AIIRILQQL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Donor MHC A*0201, A32, B49, B51, Cw1, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins

References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location Vpr (59–67)
Author Location Vpr (59–)
Epitope AIIRILQQL
Epitope name AL9
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords acute infection
References Goulder *et al.* 2001a

- Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia.
- A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation.

HXB2 Location Vpr (59–67)
Author Location Vpr (59–67 SF2)
Epitope AIIRILQQL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 0/6 group 2, and 0/4 group 3.

HXB2 Location Vpr (59–67)
Author Location
Epitope AIIRILQQL
Epitope name Vpr-AL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A02, 4/35 (11%) recognized this epitope.

HXB2 Location Vpr (59–67)
Author Location Vpr (59–67)
Epitope AIIRILQQL
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

HXB2 Location Vpr (62–70)
Author Location Vpr (62–)
Epitope RILQQLLFI
Epitope name Vpr-62
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- This epitope binds to three HLA-A2 supertype alleles: A*0202, A*6802 (strongest affinity) and A*0203.
- 3/22 chronically infected patients had a weak ELISPOT response to this epitope.
- 0/12 HLA-A2 patients with acute HIV-1 infection responded to this peptide.

HXB2 Location Vpr (62–70)

Author Location Vpr (62–70)
Epitope RILQQLLFI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vpr (62–70)
Author Location Vpr
Epitope RILQQLLFI
Epitope name Vpr 62
Subtype M
Immunogen Vaccine, in vitro stimulation or selection *Vector/Type:* DNA, peptide *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, mouse, humanized mouse (A*0201)
Assay type cytokine production, T-cell Elispot
Keywords inter-clade comparisons, computational epitope prediction, escape, TCR usage, variant cross-recognition or cross-neutralization
References McKinney *et al.* 2004

- This study examined variant recognition of epitopes presented by A*0201 and A*1101. Numerous amino acid substitutions can be introduced into epitopes without disrupting their recognition by CTLs, although epitopes with multiple substitutions were less recognized. An algorithm was constructed for prediction of epitopes capable of inducing responses to a great number of variant epitopes.
- A total of 23 variant forms of Vpr 62 were identified. More than 95% of the variant epitopes were recognized by CTLs from mice immunized with the parental form.
- Vpr 62 epitope (parent or variant form) was present in 96% of HIV sequences of many M group subtypes.

HXB2 Location Vpr (62–70)
Author Location Vpr (62–70)
Epitope RILQQLLFI
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

HXB2 Location Vpr
Author Location
Epitope
Immunogen Vaccine
Vector/Type: adenovirus *HIV component:* Gag-Pol, Nef, Vpr
Species (MHC) mouse
References Muthumani *et al.* 2002

- Vpr can cause cells to go into G2 arrest, and it surpresses immune cell activation and inflammatory cytokine production, so co-immunization of BALB/c mice with recombinant adenovirus expressing Vpr and HIV-1 antigens Nef or Gag/Pol was tested to see if Vpr reduced the immune response to the other HIV antigens.
- Vpr compromised CD8+ T-cell lytic responses and T-helper proliferative responses in mice co-immunized with Vpr and Nef or Gag/Pol.
- In vitro, Vpr reduced T-cell cytokine production of IL-12 and TNFalpha, indicative of Vpr-mediated immune suppression.

II-B-16 Tat CTL, CD8+, epitopes

HXB2 Location Tat (2–11)
Author Location
Epitope WPVDPRLEPW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then

compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Tat (2–11)
Author Location
Epitope EPVDPRLEPW
Epitope name Tat-EW10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5301)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B*5301, 3/15 (20%) recognized this epitope.

HXB2 Location Tat (2–11)
Author Location (C consensus)
Epitope EPVDPNLEPW
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*5301)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Tat (2–11)
Author Location (LAI)
Epitope EPVDPRLEPW
Subtype B
Immunogen
Species (MHC) (B53)
Keywords optimal epitope
References Addo *et al.* 2001; Frahm *et al.* 2004

HXB2 Location Tat (2–11)
Author Location Tat (2–11 BRU)
Epitope EPVDPRLEPW
Epitope name Tat 1
Immunogen HIV-1 infection
Species (MHC) human (B53)
References Addo *et al.* 2001

- Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides.
- 11/57 (19.3%) HIV-1 + individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide.
- EPVDPRLEPW was recognized by four individuals, but only two were B53, thus this epitope can probably be presented by other HLA alleles.

HXB2 Location Tat (2–11)
Author Location Tat (2–11)
Epitope EPVDPRLEPW
Immunogen HIV-1 infection
Species (MHC) human (B53)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Tat (2–11)
Author Location Tat
Epitope EPVDPRLEPW
Epitope name EW10
Immunogen HIV-1 infection
Species (MHC) human (B53)
Assay type Chromium-release assay, Flow cytometric CTL assay
Keywords class I down-regulation by Nef
References Bobbitt *et al.* 2003

- Nef, through Nef-mediated MHC-1 down-regulation, is not the only viral protein to influence levels of HIV-specific CTL recognition. The Rev L60F mutation, a common natural variant, can decrease CTL recognition of late gene products. The Rev mutation impacts the early to late gene switch, reducing late gene product production (Gag, Pol, Env, Vpu, Vpr and Vif), while increasing Nef production, both of which reduce the impact CTL recognition of late gene products. As expected, Rev L60F rendered HIV infected cells more resistant to CTL that recognized epitopes from the late proteins Env and Gag. Gag expression is reduced more than Env, and Gag-specific CTL were more profoundly affected. Conversely CTL against an epitope in an early gene product, Tat, were more effeciently recognized when infected with viruses carrying the Rev L60F mutation.
- Patients in the asymptomic phase with active immune responses had more CTL resistant viruses, with lower Rev activity, lower Gag expression and greater resistance to Gag-specific CTL killing, while viruses isolated from people with AIDS were more sensitive to CTL killing.

HXB2 Location Tat (12–21)
Author Location Tat (12–21 SUMA)
Epitope KHPGSQPKTA
Epitope name Tat KA10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.

Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location Tat (16–30)
Author Location Tat (16–30)
Epitope SQPKTACNKCYCKRC
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Tat (17–26)
Author Location
Epitope QPKTACTTCY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Tat (17–26)
Author Location Tat (17–26)
Epitope QPKTACTTCY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Tat (20–28)
Author Location Tat
Epitope TACNNCYCK
Epitope name 1342
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A23, B49, B57, C?
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for TACNNCYCK: 46%

HXB2 Location Tat (20–29)
Author Location Tat
Epitope TACNNCYCKK
Epitope name 1279
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A68)
Donor MHC A01, A68, B15, B40, Cw03

Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for TACNNCYCKK:74%. This peptide bound A68, not A11.

HXB2 Location Tat (24–32)
Author Location Tat (24–32 BORI)
Epitope NCYCKKCCY
Epitope name Tat NY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2902)
Donor MHC A*2902, B*1402, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, acute infection, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient BORI had high viral loads and rapid CD4 decline. BORI mounted 8 detected responses. BORI did not control viral replication well, and escape mutations occurred early and in most epitopes, 6/7 that were precisely identified.
- There were five variants of the NCYCKKCCY epitope in BORI, and new changes kept accruing. kCYCKKCCY was apparent by day 31, kCYCKrCCY by day 218, and kCYCKqCCY by day 556; all conferred escape, the double mutants abrogating the response. NCYCKKyCY and NCYCKKCCc were also transiently present at day 55, but were not tested for CTL escape.

HXB2 Location Tat (24–32)
Author Location Tat (24–32 WEAU)
Epitope NCYCKRCCF
Epitope name Tat NF9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2902)
Donor MHC A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- There was a weak response to this epitope during acute infection that was lost by early infection. The epitope variant kCYCKRCCF was evident by day 72, and other variants were evident in samples taking at 391 and 772 days, including NCYCKkCCF,tCYCKRCCF, kCYCKsCCF and kCYCKkCCF. It was not determined if these were specifically escape mutations, but the CTL response diminished in vivo as kCYCKRCCF variant came up.

HXB2 Location Tat (30–37)
Author Location Tat (30–37)
Epitope CCFHCQVC
Immunogen
Species (MHC) human (Cw*12)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Tat (30–37)
Author Location Tat (30–37)
Epitope CCFHCQVC
Immunogen HIV-1 infection
Species (MHC) human (Cw*1203)
Donor MHC A3, A26, B7, B*3801, Cw*0702, Cw*1203; A*0201, A*2501, B18, B51, Cw*0102, Cw*1203
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early treatment
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes

to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- Two individuals recognized this epitope both presented by Cw*1203.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.

HXB2 Location Tat (30–37)
Author Location Tat (30–37)
Epitope CCFHCQVC
Immunogen HIV-1 infection
Species (MHC) human (Cw*1203)
Donor MHC A3, A26, B7, B*3801, Cw*0702, Cw*1203; A*0201, A*2501, B18, B51, Cw*0102, Cw*1203
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early treatment
References Cao *et al.* 2003

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- Two individuals recognized this epitope both presented by Cw*1203.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.

HXB2 Location Tat (32–41)
Author Location Tat (32–41 SUMA)
Epitope FHCQVCFMTK
Epitope name Tat FK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, epitope processing, immunodominance, escape, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time. Early in infection, three overlapping epitopes in Tat carried mutations: FHCQVCFMTK, VCFMTKGLGI, and MTKGLGISY. An M->T substitution was evident during acute infection in the first sample, at four days of the onset of symptoms, and a rare second variant was seen at day 20 that added a K->E substitution. The M->T substitution abrogated responses to FHCQVCFtTK, VCFtTKGLGI, but not in the third epitope tTKGLGISY. By day 69 a double mutation was evident that persisted through day 435, F->L and T->K. Variants lHCQVCFMkK, VCFMkKGLGI were not recognized,and impact processing of the MkKGLGISY epitope.

HXB2 Location Tat (36–45)
Author Location Tat (36–45 SUMA)
Epitope VCFMTKGLGI
Epitope name Tat VI10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1501)
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, epitope processing, immunodominance, escape, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.

- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time. Early in infection, three overlapping epitopes in Tat carried mutations: FHCQVCFMTK, VCFMTKGLGI, and MTKGLGISY. An M->T substitution was evident during acute infection in the first sample, at four days of the onset of symptoms, and a rare second variant was seen at day 20 that added a K->E substitution. The M->T substitution abrogated responses to FHCQVCFtTK, VCFtTKGLGI, but not in the third epitope tTKGLGISY. By day 69 a double mutation was evident that persisted through day 435, F->L and T->K. Variants lHCQVCFMkK, VCFMkKGLGI were not recognized,and impact processing of the MkKGLGISY epitope.

HXB2 Location Tat (36–50)
Author Location (subtype C)
Epitope VCFQTKGLGISYGRK
Subtype C
Immunogen
Species (MHC) human
Keywords immunodominance, escape
References Novitsky *et al.* 2001

- This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort.
- 17 of 46 patient reacted with Tat immunodominant peptide VCFQTKGLGISYGRK.
- Most of the CTL responses occurred despite a mismatch between the autologous viral sequence and peptide – complete matches were seen only in 4 of 19 cases (21%) and the mismatched CTL tended not to respond to the autologous viral peptide indicative of immune escape.

HXB2 Location Tat (36–50)
Author Location Tat (36–50)
Epitope VCFQTKGLGISYGRK
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Tat (36–52)
Author Location Tat
Epitope VCFTTKALGISYGRKKR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 28% (19/70) targeted one or more Tat peptides, and this peptide was the most frequently recognized epitope in Tat (27%).
- The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.

HXB2 Location Tat (38–47)
Author Location (subtype C)
Epitope FQTKGLGISY
Epitope name T38-FY10
Subtype C
Immunogen
Species (MHC) human (B*1503)
Keywords immunodominance
References Novitsky *et al.* 2001

- This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort.
- 17 of 46 patient reacted with Tat immunodominant peptide VCFQTKGLGISYGRK.
- FQTKGLGISY was the optimal epitope in the peptide VCFQTKGLGISYGRK among B*1503+ individuals.

HXB2 Location Tat (38–47)
Author Location Tat (38–47)
Epitope FQTKGLGISY
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Tat (38–47)
Author Location (C consensus)
Epitope FQTKGLGISY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Tat (39–47)
Author Location Tat (39–47 SUMA)
Epitope MTKGLGISY
Epitope name Tat MY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1501)
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, epitope processing, immunodominance, escape, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time. Early in infection, three overlapping epitopes in Tat carried mutations: FHCQVCFMTK, VCFMTKGLGI, and MTKGLGISY. An M->T substitution was evident during acute infection in the first sample, at four days of the onset of symptoms, and a rare second variant was seen at day 20 that added a K->E substitution. The M->T substitution abrogated responses to FHCQVCFtTK, VCFtTKGLGI, but not in the third epitope tTKGLGISY. By day 69 a double mutation was evident that persisted through day 435, F->L and T->K. Variants lHCQVCFMkK, VCFMkKGLGI were not recognized, but the CTL response was strong to MkKGLGISY. The authors provide evidence that the F->L and T->K substitutions impact processing of the MTKGLGISY epitope, as the mutations don't abrogate a CTL response to the peptide, but Tat expressed in target cells doesn't allow recognition of the Tat variant.
- MTKGLGISY was the highest level response in acute and early infection.

HXB2 Location Tat (39–49)
Author Location Tat (38–48)
Epitope ITKGLGISYGR
Epitope name Tat-4.8
Immunogen HIV-1 infection
Species (MHC) human (A*6801)
Keywords assay standardization/improvement
References Oxenius *et al.* 2002a

- This epitope and HLA-A*6801 presenting molecule were rapidly defined using a modified Elispot assay.
- The 11-mer is the optimal epitope but A*6801 epitopes tolerate length variation.

HXB2 Location Tat (39–49)
Author Location Tat (39–49)
Epitope ITKGLGISYGR
Immunogen HIV-1 infection
Species (MHC) human (A*6801)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Tat (39–49)
Author Location Tat (38–48)
Epitope ITKGLGISYGR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A68)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Tat (39–49)
Author Location Tat (38–48)
Epitope ITKGLGISYGR
Epitope name ITK
Immunogen HIV-1 infection
Species (MHC) human (A68.1)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This was one of 8 reactive epitopes found not to vary over time.

HXB2 Location Tat (40–49)
Author Location
Epitope TKALGISYGR
Subtype B

Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Tat (49–57)
Author Location Tat (49–57)
Epitope RKKRRQRRR
Immunogen
Species (MHC) mouse
References Kim *et al.* 1997a

- The Tat peptide RKKRRQRRR when conjugated to a protein can cause that protein to be taken up by APCs and presented to CTL.
- The system was demonstrated by vaccinating mice with an OVA-Tat peptide conjugate and immunizing H-2 K^b mice.
- The CTL response to the H-2 K^b specific OVA peptide SIINFEKL was stimulated.

HXB2 Location Tat (49–57)
Author Location Tat (49–57)
Epitope RKKRRQRRR
Immunogen Vaccine
Vector/Type: DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18
Species (MHC) mouse (H-2^d)
Keywords Th1
References Billaut-Mulot *et al.* 2001

- DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization.
- Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost.
- Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-gamma)
- Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.

HXB2 Location Tat (83–92)
Author Location Tat
Epitope GPKESKKKVE
Immunogen
Species (MHC) human (B58)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay.
- GPKESKKKVE was newly identified as an HLA-B58 epitope in this study.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat
Species (MHC) human
Keywords HAART, ART
References Calarota *et al.* 1999

- 9/9 HIV-1 + subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated.
- The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses.
- Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Froebel *et al.* 1997

- Two HIV-1 infected children with contrasting disease courses were followed longitudinally – one died of AIDS, the other is a long-term non-progressor.
- Reactivity against Gag, Pol, Env and Tat proteins was tested by PBMC bulk cultured cells reacting with protein expressed in vaccinia constructs in autologous EBV transformed B cells.
- The child who progressed consistently had CTL against Pol and Tat.

- The long-term non-progressing child had no detectable CTL, but was heterozygous for a mutation in the CCR5 receptor and for HLA-B49, which has been shown to be associated with slower progression.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS)
Species (MHC) human
Keywords review
References Calarota & Wahren 2001

- This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asymptomatic HIV+ individuals.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade BH10 *HIV component:* Tat *Adjuvant:* Immune stimulating complexes (ISCOM), CpG immunostimulatory sequence (ISS)
Species (MHC) macaque
References Cafaro *et al.* 2001

- Macaques (macaca fascicularis) were immunized with HIV-1 Tat on an adenovirus major late promotor in a plasmid with 23 CpG sequences, 12 unmethylated.
- The vaccinated animals contained a primary infection challenge with SHIV89.6P, preventing CD4+ T-cell decline in the animals, suggesting Tat may be useful at blocking viral replication at its early stage.

HXB2 Location Tat
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References Aldhous *et al.* 1994; Kuhn *et al.* 2002

- Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points.
- Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses to Tat (1/2), Pol (2/2), Gag (1/2).
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen HIV-1 infection, Vaccine

Species (MHC) human
Keywords review, escape, early-expressed proteins
References Gruters *et al.* 2002

- This paper is a review that makes a case for using Tat and Rev as part of a vaccine strategy.
- CTL against Tat and Rev were found preferentially in long term non-progressors.
- Tat/Rev vaccinations of macaques provided protection or reduction in viremia, with high levels of CTL providing protection from challenge, lower levels of CTL having lower viremia, while Gag/Pol vaccinations with did not result in decreased viremia.
- Early expression of Tat/Rev may in part explain the enhanced benefit of a CTL response directed at these proteins, and CTL escape is more prominent in these proteins.

HXB2 Location Tat
Author Location Tat (BH10)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade BH10 *HIV component:* Tat *Adjuvant:* cationic block copolymer K2
Species (MHC) mouse
Donor MHC H-2d
Assay type proliferation, Chromium-release assay
References Caputo *et al.* 2003

- Mice were immunized intramuscularly with a plasmid DNA vaccine (HIV-1 pCV-tat DNA) alone or complexed with a cationic block polymer K1, K2, or K5, which block digestion by DNAase I and enhance DNA delivery to APC.
- CTL responses to low dose Tat DNA vaccination with K2 were greatly enhanced relative to responses to DNA alone.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen Vaccine
Vector/Type: DNA, protein *HIV component:* Tat *Adjuvant:* aluminum hydroxide, Ribi adjuvant (MPL+TDM) (RIBI)
Species (MHC) macaque
Keywords review, early-expressed proteins
References Fanales-Belasio *et al.* 2002a

- HIV-1 Tat protein is efficiently taken up by monocyte-derived dendritic cells (MDDCs) and promotes Th1 immune responses. A Tat based vaccine can elicit an immune response that can control primary infection in monkeys that are in early stage of in infection with SHIV89.6P.
- Tat-specific CTL activity was detected in four monkeys inoculated with i.m. with pCV-tat.

HXB2 Location Tat
Author Location
Epitope
Immunogen in vitro stimulation or selection
Species (MHC)

Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords epitope processing, immunodominance, early-expressed proteins, Th1, adjuvant comparison
References Gavioli *et al.* 2004

- HIV-1 Tat protein modulates proteasome composition and activity in B and T cells that either express Tat or are treated with exogenous biologically active Tat protein. This results in modification of Ag processing where presentation of immunodominant EBV epitopes is decreased and presentation of subdominant epitopes is increased. The authors suggest that the immunomodulatory effects of endogenous and exogenous Tat may be beneficial in terms of expanding stimulation of responses to subdominant epitopes, and may be useful as an adjuvant.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen Vaccine
Vector/Type: adeno-associated virus (AAV) *HIV component:* Env, Rev, Tat *Adjuvant:* IL-2
Species (MHC) mouse (H-2^d)
References Xin *et al.* 2001

- An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice.
- A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL.
- Boosting enhanced the humoral response, and IL2 enhanced T-cell immunity.

HXB2 Location Tat
Author Location Tat (IIIB)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide (MALP)
Species (MHC) mouse (H-2^d)
Assay type T-cell Elispot
References Borsutzky *et al.* 2003

- BALB/c mice that were vaccinated intranasally with Tat protein plus mucosal adjuvant macrophage-activating lipopeptide-2 (MALP-2) had increased proliferative, antibody, and IFN-gamma producing T-cell responses than did mice with Tat+IFA delivered by the i.p. route.
- IFA as adjuvant stimulated a Th2-dominant response pattern, and MALP-2 as adjuvant shifted to a Th1 response. In animals vaccinated with Tat+MALP-2, IFN-gamma and IL-2 were the most prominent cytokines, with some IL-6. In contrast, in mice vaccinated with Tat+IFA, IL-6 was the dominant cytokine. Secreted IL-4, IL-5 and IL-10 were below the detection limit in both cases.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen Vaccine
Vector/Type: protein *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA), red blood cells
Species (MHC) mouse (H-2^d)
Assay type Chromium-release assay
Keywords dendritic cells, Th1, Th2, immunotherapy
References Dominici *et al.* 2003

- BALB/c mice were immunized with Tat protein bound to red blood cells via biotin-avidin conjugation. This antigen delivery system was successfully internalized by dendritic cells, and induced more consistent anti-Tat Abs responses and sightly increased Tat-specific CTL responses relative to Tat with CFA.

II-B-17 Rev CTL, CD8+, epitopes

HXB2 Location Rev (9–23)
Author Location Rev (9–23 HXB2)
Epitope DEELIRTVRLIKLLY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Blazevic *et al.* 1995

- Induces both Th and CTL activities, no HLA restriction analysis performed.

HXB2 Location Rev (11–23)
Author Location Rev (14–23)
Epitope KAVRRLIKFLY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Rev (11–23)
Author Location Rev (14–23)
Epitope KAVRRLIKFLY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5801)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.

- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Rev (12–31)
Author Location Rev (11–30 SF2)
Epitope LLKAVRLIKFLYQSNPPPNF
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Only one subject had CTL that could recognize vaccinia-expressed LAI Rev.
- This subject had a CTL response to this peptide, and was HLA-A2, A24, B13, B35.

HXB2 Location Rev (14–23)
Author Location
Epitope KAVRLIKFLY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Rev (14–23)
Author Location Rev (14–23 subtype B)
Epitope KAVRLIKFLY
Subtype B
Immunogen
Species (MHC) human (B*5701)
Keywords optimal epitope
References Addo *et al.* 2001; Frahm *et al.* 2004

- C. Brander notes this is a B*5701 epitope.

HXB2 Location Rev (14–23)
Author Location Rev (14–23 BRU)
Epitope KAVRIKLFLY
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords cross-presentation by different HLA
References Addo *et al.* 2001

- Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides.
- 11/57 (19.3%) HIV-1 + individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide.
- This epitope was also recognized by another individual in whom it was restricted by HLA*B5801, an allele closely related to HLA*B5701, suggesting cross-presentation by the two HLA alleles.

HXB2 Location Rev (14–23)
Author Location Rev (14–23 subtype B)
Epitope KAVRLIKFLY
Subtype B
Immunogen
Species (MHC) human (B*5801)
Keywords optimal epitope
References Addo *et al.* 2001; Frahm *et al.* 2004

- C. Brander notes this is a B*5801 epitope.

HXB2 Location Rev (14–23)
Author Location Rev (14–23 BRU)
Epitope KAVRIKLFLY
Immunogen HIV-1 infection
Species (MHC) human (B*5801)
Keywords cross-presentation by different HLA
References Addo *et al.* 2001

- Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides.
- 11/57 (19.3%) HIV-1 + individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide.
- This epitope was also recognized by another individual in whom it was restricted by HLA*B5701, an allele closely related to HLA*B5801, suggesting cross-presentation by the two HLA alleles.

HXB2 Location Rev (20–28)
Author Location Rev
Epitope KILYQSNPY
Epitope name 1341
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A02, A03, B08, B51, Cw01, Cw07
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for KILYQSNPY: 36%

HXB2 Location Rev (25–39)
Author Location Rev (25–39 HXB2)
Epitope SNPPPNPEGTRQARR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Blazevic *et al.* 1995

- Induces both Th and CTL activities, no HLA restriction analysis performed.

HXB2 Location Rev (33–48)
Author Location Rev (33–48 HXB2)
Epitope GTRQARRNRRRRWRER
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Blazevic *et al.* 1995

- Induces both Th and CTL activities, no HLA restriction analysis performed.

HXB2 Location Rev (41–56)
Author Location Rev (41–56 HXB2)
Epitope RRRRWRERQRQIHSIS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Blazevic *et al.* 1995

- Induces both Th and CTL activities.

HXB2 Location Rev (55–63)
Author Location Rev (55–63 LAI)
Epitope ISERILSTY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A1)
Keywords rate of progression
References van Baalen *et al.* 1997

- Predicted to be an HLA-A1 epitope based on anchor residues 2S and 9Y.
- Both forms LSGWL(L or I)STY, with intact anchors, were found in an HLA-A1+ individual with Rev-responsive CTL.
- An HLA-A1 individual who did not make a Rev response had lost the C-term anchor, ISGWILS(T or N)S.
- 3/7 long-term non-progressors and 0/5 progressors were positive for HLA-B57 (associated with prolonged survival)
- CTLp frequencies to Rev and Tat were inversely correlated with rapid progression to AIDS, but not Gag, RT or Nef.

HXB2 Location Rev (55–63)
Author Location Rev (55–63)
Epitope ISERILSTY
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A1)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location Rev (55–63)
Author Location RT Pol (55–63)
Epitope ISERILSTY
Immunogen HIV-1 infection
Species (MHC) human (A1)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 8/13 patients recognized this epitope, itw was the most commonly recognized of three A*01 epitopes tested.

HXB2 Location Rev (57–66)
Author Location
Epitope ERILSTYLGR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then

compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Rev (57–66)
Author Location Rev (57–66)
Epitope ERILSTYLGR
Immunogen HIV-1 infection
Species (MHC) human (A*03)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Rev (57–66)
Author Location Rev (57–66)
Epitope ERILSTYLGR
Epitope name A3-ER10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals had detectable responses to this epitope after STI.

HXB2 Location Rev (58–66)
Author Location Rev (58–66)
Epitope RILSTYLGR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Rev (66–73)
Author Location Rev (66–)
Epitope RSAEPVPL
Epitope name Rev66
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Rev *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a low A2-binder, and induced a CTL responses in 1/6 A2 transgenic mice. Responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.

HXB2 Location Rev (66–81)
Author Location Rev
Epitope RSAEPVPLQLPPLERL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 36% (25/70) targeted one or more Rev peptides, and this peptide was the most frequently recognized epitope in Rev (32%).
- The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.

HXB2 Location Rev (67–75)
Author Location
Epitope SAEPVPLQL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint

on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Rev (67–75)
Author Location Rev (65–77 BH10, LAI)
Epitope SAEPVPLQL
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002
- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is GRSAEPVPLQLPP) has similarity with transforming growth factor beta binding protein protein I, fragment ARSAEPEVATAPP.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is EPVPLQLPPL) also has similarity with the epidermal growth factor receptor substrate 15, fragment EPVPMSLPPA.

HXB2 Location Rev (67–75)
Author Location (LAI)
Epitope SAEPVPLQL
Subtype B
Immunogen
Species (MHC) (B14)
References van Baalen & Gruters 2000

HXB2 Location Rev (67–75)
Author Location Rev
Epitope SAEPVPLQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords escape
References Schutten *et al.* 2001
- Molecularly cloned primary NSI macrophage tropic strain 2.1 and SI non-macrophage tropic strain 1.2 were isolated from study participant ACH320 and use to infect irradiated XID mice that had been reconstituted with human PBMC from B14+ seronegative donors – results indicate CTL may favor selective outgrowth of macrophage tropic strains.
- The CTL clone TCC108 specific for SAEPVPLQL, previously described by van Baalen 1997, and van Baalen 1998, was stimulated *in vitro* and given to the mice to apply specific CTL pressure.
- The macrophage-tropic HIV-1 strain #2.1 escaped CTL pressure more efficiently (7/14 animals) than its non-macrophage-tropic counterpart #1.2(SI) – the latter isolate was suppressed in 13/14 animals – macrophage may serve as a CTL sanctuary and reduced pressure on macrophage tropic HIV strains may allow additional replication to assist with acquisition of escape.
- Specific HIV-1 variants selectively induced by TCC108 were for strain 1.2: SEEPVPLQL, and for strain 2.1: SAEHVPLQL, SAESVPLQL, SVEPVPLQL, SLEPVPLQL, SAEPVPFQL, and SAEPVPFQL.

HXB2 Location Rev (67–75)
Author Location Rev (67–75)
Epitope SAEPVPLQL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords acute infection, early-expressed proteins, kinetics
References van Baalen *et al.* 2002
- Tat, Rev and Nef are the first HIV proteins expressed upon acute infection of T-cells (< 6 hours), and RT is not expressed until after 24 hours. The B14-restricted Rev-SAEPVPLQL specific CD8 T-cell clone TCC108, and the B57-restricted RT-IVLPEKDSW specific CD8 T-cell clone TCL1C11 were co-incubated with CD4+ cultures innoculated with HIV-1 at low MOI. Co-incubation with the Rev-specific CTL resulted in two logs less HIV-1 production in ten days of culture. When the RT epitope was cloned into the Nef gene of the infecting strain, another early expressed protein, it proved as effective as the Rev epitope at inhibiting viral production. A mathematical model of CTL-target interactions suggest early proteins are important for vaccine design.

HXB2 Location Rev (67–75)
Author Location Rev (67–75)
Epitope SAEPVPLQL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords early-expressed proteins
References Addo *et al.* 2002b
- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Rev (67–75)
Author Location Rev (67–75 IIIB)
Epitope SAEPVPLQL
Immunogen HIV-1 infection
Species (MHC) human (B14, Cw8)
References van Baalen *et al.* 1998
- The Rev-specific CTL response studied here was from an individual infected with HIV-1 for more than 12 years without developing symptoms – Rev and Tat are expressed early and CTL activity against these proteins has been correlated with long-term survival.
- The CTL clone TCC108 specific for this epitope was studied *in vitro*.

- CTLs added immediately after infection suppressed viral production, indicative of CTL interference with viral production prior to lysis – CTL-mediated lysis occurred after the onset of progeny viral release, but prior to peak viral production.
- Rapid selection of a E69K mutation, which abolished CTL, recognition was observed.
- The epitope was originally listed as B14, but Cw8 and B14 are in linkage disequilibrium, and in this case were not distinguished (pers. comm., Christian Brander, 1999)

HXB2 Location Rev (67–75)
Author Location (LAI)
Epitope SAEPVPLQL
Subtype B
Immunogen
Species (MHC) human (Cw*0501)
Keywords optimal epitope
References Addo *et al.* 2001; Frahm *et al.* 2004

HXB2 Location Rev (67–75)
Author Location Rev (SF2)
Epitope SAEPVPLQL
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (Cw5)
Keywords acute infection
References Goulder *et al.* 2001a

- Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia.
- A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation.

HXB2 Location Rev (67–75)
Author Location Rev (67–75 SF2)
Epitope SAEPVPLQL
Immunogen HIV-1 infection
Species (MHC) human (Cw5)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-Cw5+ individuals that had a CTL response to this epitope broken down by group: 2/6 group 1, 0/1 group 2, and 0/2 group 3.

HXB2 Location Rev (67–75)
Author Location Rev (67–75)
Epitope SAEPVPLQL
Immunogen HIV-1 infection
Species (MHC) human (Cw5)
Donor MHC A1, A*0201, B44, B57, Cw5, Cw6
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location Rev (67–75)
Author Location Rev (67–75)
Epitope SAEPVPLQL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw5, Cw8)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Rev (67–75)
Author Location Rev (69–77 BRU)
Epitope SAEPVPLQL
Epitope name Rev SL9
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
Keywords HAART, ART, supervised treatment interruptions (STI), acute infection
References Addo *et al.* 2001

- Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides.

- 11/57 (19.3%) HIV-1 + individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide.
- This epitope is the first HIV-specific CTL epitope resticted by HLA-Cw5.
- This epitope was recognized by 2/5 individuals expressing HLA-Cw8 and by 5/11 individuals expressing Cw5 allele, which differs from Cw8 by 4 amino acids, suggesting promiscuous presentation of the epitope between those HLA molecules.
- Longitudinal data was available for 6 Rev-SL9 responders, who were treated during acute infection, and the response was stable 2 and 12 months after initiaion of HAART, measurements by ELISPOT and flow-based intracellular cytokine staining (ICS) were concordant – in two subjects the response was heightened by transient reexposure to antigen with treatment interruption at 12 to 14 months.

HXB2 Location Rev (73–81)
Author Location Rev (73–)
Epitope LQLPPIERL
Epitope name Rev73
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Rev
Adjuvant: Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced CTL responses in mice. Responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.

HXB2 Location Rev (75–83)
Author Location
Epitope LPPLERLTL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.
- What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.

HXB2 Location Rev (96–104)
Author Location Rev (96–)
Epitope GMGSPQILV
Epitope name Rev96(2M)
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Rev
Adjuvant: Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was an intermediate A2 binder, and induced a CD8+ T-cell IFN gamma response in 1/6 mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.
- The variant gVgspqilv did not elicit a CD8+ T-cell IFN gamma response in transgenic mice, and bound to A2 with low affinity.

HXB2 Location Rev (102–110)
Author Location Rev (102–)
Epitope ILVESPAVL
Epitope name Rev102
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Rev
Adjuvant: Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder that did not induce CTL or CD8+ T-cell IFN gamma responses in mice, but responses were detected in 2/17 HIV+ HLA-A2 subjects.

HXB2 Location Rev (107–116)
Author Location Rev
Epitope PTVLESGTKE
Epitope name 1277
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A68)
Donor MHC A11, A68, B42, B45, Cw16, Cw17
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for PTVLESGTKE:16%. This epitope can be presented by A68, but did not bind to A11.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat
Species (MHC) human
Keywords HAART, ART
References Calarota *et al.* 1999

- 9/9 HIV-1 + subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated.
- The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses.
- Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.

HXB2 Location Rev
Author Location (subtype C)
Epitope
Subtype C
Immunogen
Species (MHC) human
References Novitsky *et al.* 2001

- This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort.
- Anti-Rev CTL responses were distributed throughout the protein and 27 of 47 subjects (57%) demonstrated HIV-1C Rev-specific ELISPOT CTL responses of more than 100 SFC/106 PBMC.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS)
Species (MHC) human
Keywords review
References Calarota & Wahren 2001

- This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asymptomatic HIV+ individuals.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen HIV-1 infection, Vaccine

Species (MHC) human
Keywords review, escape, early-expressed proteins
References Gruters *et al.* 2002

- This paper is a review that makes a case for using Tat and Rev as part of a vaccine strategy.
- CTL against Tat and Rev were found preferentially in long term non-progressors.
- Tat/Rev vaccinations of macaques provided protection or reduction in viremia, with high levels of CTL providing protection from challenge, lower levels of CTL having lower viremia, while Gag/Pol vaccinations with did not result in decreased viremia.
- Early expression of Tat/Rev may in part explain the enhanced benefit of a CTL response directed at these proteins, and CTL escape is more prominent in these proteins.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen Vaccine
Vector/Type: DNA with CMV promotor with cationic liposome *HIV component:* gp160, Rev
Species (MHC) mouse (H-2^d)
References Ishii *et al.* 1997

- pCMV160/Rev is a DNA vaccine candidate carrying gp160 and Rev linked to a cytomegalovirus (CMV promotor)
- pCMV160/Rev given in conjunction with a cationic liposome gave enhanced DTH, Ab and CTL responses.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Rev *Adjuvant:* CD40
Species (MHC) mouse (H-2^d)
Keywords Th1, Th2
References Ihata *et al.* 1999

- pcRev DNA i.m. vaccination in BALB/c mice induced Th1, Th2 and IgG responses, and enhanced the CTL response to Rev, but did not induce mucosal IgA.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen Vaccine
Vector/Type: adeno-associated virus (AAV) *HIV component:* Env, Rev, Tat *Adjuvant:* IL-2
Species (MHC) mouse (H-2^d)
References Xin *et al.* 2001

- An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice.
- A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL.
- Boosting enhanced the humoral response, and IL2 enhanced T-cell immunity.

II-B-18 Vpu CTL, CD8+, epitopes

HXB2 Location Vpu (4–13)
Author Location Vpu
Epitope LVILAIVALV
Immunogen
Species (MHC) human (B7)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay.
- LVILAIVALV was newly identified as an HLA-B7 epitope in this study using ELISPOT, but could not be shown to bind to B7.

HXB2 Location Vpu (4–13)
Author Location Vpu
Epitope LVILAIVALV
Epitope name 1300
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A03, A24, B07, B38, Cw07, Cw12/13
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for LVILAIVALV: 6%

HXB2 Location Vpu (13–21)
Author Location Vpu (13–)
Epitope VVAAIIAIV
Epitope name Vpu13
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Vpu *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was an intermediate A2 binder that did not induce CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.

HXB2 Location Vpu (25–40)
Author Location Vpu
Epitope IVFIEYRKLRQRKID
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – only 2% (2/70) targeted one or more Vpu peptides, including this peptide.
- The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.

HXB2 Location Vpu (29–37)
Author Location Vpu (29–37)
Epitope EYRKILRQR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*3303)
Keywords early-expressed proteins
References Addo *et al.* 2002b

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.
- 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.
- All known optimally defined epitopes were summarized for the five proteins.

HXB2 Location Vpu (29–37)
Author Location Vpu (29–37)
Epitope EYRKILRQR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*3303)
Keywords early-expressed proteins
References Addo *et al.* 2002a

- Detection of HIV CTL epitopes is rare in Vpu, and this is the first optimally defined Vpu epitope.
- This CTL response was first detected in a long term non-progressor, and 3/6 HLA A*3303 positive individuals were found to have a CTL response to this epitope.
- HLA A*3303 is common in West Africa and Asia.

HXB2 Location Vpu (29–37)
Author Location Vpu (29–37)
Epitope EYRKILRQR
Immunogen HIV-1 infection
Species (MHC) human (A*3303)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Vpu
Author Location Vpu
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Vif, Vpu
Species (MHC) mouse (H-2^d)
Keywords inter-clade comparisons, Th1
References Ayyavoo *et al.* 2000

- Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels.
- Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response.
- IL-4 production was not significantly changed after antigen stimulation compared to control levels.
- Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization-stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.

II-B-19 gp160 CTL, CD8+, epitopes

HXB2 Location gp160 (2–10)
Author Location gp160 (2–10 IIIB)
Epitope RVKEKYQHL
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0801 epitope.

HXB2 Location gp160 (2–10)
Author Location gp160 (2–10 IIIB)
Epitope RVKEKYQHL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords inter-clade comparisons
References Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.
- Type-specific epitope, unique to the LAI and IIIB because of a deletion of three amino acids that are present in all other subtype B HIV-1s.
- RVKGIRKNYQHL, a variant found in JRCSF, was not recognized.
- This epitope is in the signal sequence of gp120.

HXB2 Location gp160 (2–10)
Author Location gp120 (2–10)
Epitope RVKEKYQHL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Day *et al.* 2001

- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.

HXB2 Location gp160 (6–12)
Author Location gp120 (6–15 CM243 subtype CRF01)
Epitope TQMNWPNLWK
Epitope name E6-15
Subtype CRF01_AE
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope after a second stimulation *in vitro* gave a weak response in HEPS study subject 186 who was HLA A2/A11.

HXB2 Location gp160 (6–12)
Author Location gp120 (6–15 CM243 subtype CRF01)
Epitope TQMNWPNLWK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using Epi-Matrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.

- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it.
- This epitope was not conserved in other subtypes, and exact matches were rare.

HXB2 Location gp160 (30–40)
Author Location Env (29–39)
Epitope AAENLWVTVYY
Immunogen HIV-1 infection
Species (MHC) human (B44)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load..
- Less than 2 of 11 patients recognized this epitope.

HXB2 Location gp160 (30–49)
Author Location gp120 (1–20)
Epitope ATEKLWVTVYYGVPVWKEAT
Epitope name ATE
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This was one of 8 reactive peptides found not to vary over time. It was one of four epitopes that were not precisely defined.

HXB2 Location gp160 (30–49)
Author Location gp120
Epitope AAEQLWVTVYYGVPVWKEAT
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords TCR usage
References Weekes *et al.* 1999b

- Peptide 7035.1: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population.
- HIV CTL responses to 3 Env and 2 Gag peptides were studied.
- The clonal composition of the TCR Vβ responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ6.

HXB2 Location gp160 (31–39)
Author Location gp160 (30–38 WEAU)
Epitope AENLWVTVY
Epitope name gp160 AY9
Immunogen HIV-1 infection
Species (MHC) human (B*4403)
Donor MHC A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- This was the immunodominant response in acute infection in WEAU, and there was rapid escape in the epitope AENLWVTVY, with three variants observed by day 30 from the onset of symptoms. Additional mutations continued to develop, so that there were 9 different forms observed through the course of sampling. The variants all conferred different levels of reduction in CTL response, double mutations or anchor mutations tended to cause the greatest reduction: AaNLWVTaY, tNkWVTVY, AgNLWVTVY, AkNLWVTVY, although the double mutant tENLWVTiY elicted a very strong CTL response, suggesting it might not be an escape form.

HXB2 Location gp160 (31–39)
Author Location gp120 (30–38 SF2)
Epitope AENLWVTVY
Immunogen HIV-1 infection
Species (MHC) human (B44)
Keywords HAART, ART, acute infection

References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B44+ individuals that had a CTL response to this epitope broken down by group: 1/8 group 1, 2/3 group 2, and 3/4 group 3.

HXB2 Location gp160 (31–39)
Author Location gp120 (30–38)
Epitope AENLWVTVY
Immunogen HIV-1 infection
Species (MHC) human (B44)
References Day *et al.* 2001

HXB2 Location gp160 (31–39)
Author Location gp120
Epitope AENLWVTVY
Immunogen HIV-1 infection
Species (MHC) human (B44)
Keywords epitope processing
References Cao *et al.* 2002

- AC2 is a B44 restricted CTL clone that recognizes AENLWVTVY.
- CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.

HXB2 Location gp160 (31–39)
Author Location (B consensus)
Epitope AENLWVTVY
Epitope name AY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B44)
Donor MHC A11, A29, B08, B44, Cw4, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location gp160 (31–40)
Author Location gp160 (30–39 WEAU)
Epitope AENLWVTVYY
Immunogen HIV-1 infection
Species (MHC) human (B*4402)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4402 epitope.

HXB2 Location gp160 (31–40)
Author Location gp160 (30–39 WEAU)
Epitope AENLWVTVYY
Immunogen HIV-1 infection
Species (MHC) human (B44)
Keywords immunodominance, escape
References Borrow *et al.* 1997; Borrow & Shaw 1998; Goulder *et al.* 1997a

- Two CTL lines from the patient WEAU were studied – one had an optimal peptide of (A)AENLWVTVYY, and the other (A)AENLWVTVY, and both responded equally well with one or two N-term Alanines.
- Rapidly post-infection, a strong immunodominant response was observed against this epitope.
- The naturally occurring forms of the peptide found in WEAU were tested as targets for early WEAU CTLs – the form TENLWVTVY was as reactive as the wild type AENLWVTVY – but the forms AKNLWVTVY, AGNLWVTVY, AANLWVTVY did not serve as targets.
- The glutamic acid in the second position is a B44 anchor residue.
- Goulder *et al.* [1997a] and Borrow & Shaw [1998] are reviews of immune escape that summarizes this study in the context of CTL escape to fixation.

HXB2 Location gp160 (31–55)
Author Location gp120 (32–56 LAI)
Epitope TEKLWVTVYYGVPVWKEATTTLFCA
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (B18)
References Johnson *et al.* 1994a

- HLA restricted CTL response to epitope in HIV-1 vaccinia-env vaccinees.

HXB2 Location gp160 (31–55)
Author Location gp120 (32–56 LAI)
Epitope TEKLWVTVYYGVPVWKEATTTLFCA
Subtype B

Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (B18)
References Ferris *et al.* 1999; Hammond *et al.* 1995

- This peptide can be processed for HLA-B18 presentation by both TAP-1/2 independent and dependent pathways.

HXB2 Location gp160 (32–40)
Author Location gp160 (29–37 SUMA)
Epitope ENLWVTVYY
Epitope name GP160 EY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location gp160 (32–40)
Author Location Env (92TH023)
Epitope DNLWVTVYY
Subtype B, CRF01_AE
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost, canarypox, canarypox prime with gp160 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Pol
Species (MHC) human (B44)
Country Thailand.
Assay type Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Paris *et al.* 2004

- 21% (40/187) of Thai adults that recieved ALVAC-HIV with or without gp120 or oligomeric gp160 had a CD8+ T-cell response. HLA-B44 was positively associated with CTL responses, and A33 had a borderline significance association with response. A33/B44/DRB1*0701 is the most common haplotype in Thailand. B46, present in 30% of the population, was negatively associated with CTL responses, although it did not reach significance. HLA class I serotypes A11, A24, A33, B46 and B75 were the most common found in 245 Thai volunteers.
- 9/11 cases of pCTL activity to Env were in people with B44. The authors suggest some of the response may be directed at the previously mapped B44 Env epitope AENLWVTVYY in HXB2, DNLWVTVYY in their CRF01 ALAVC vaccine 92TH023. B*4403 is the most common B44 allele among Thais, while B*4402 is more common among Caucasians; a prior study had shown that B*4403 may be able to present a broader spectrum of epitopes than B*4402.

HXB2 Location gp160 (33–42)
Author Location gp120 (32–41 LAI)
Epitope KLWVTVYYGV
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human (A2)
References Dupuis *et al.* 1995

- CTL from HLA-A2 positive subject react with this peptide.

HXB2 Location gp160 (33–42)
Author Location Env
Epitope NLWVTVYYGV
Epitope name 1256
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A02, A30, B39,?, ?
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for NLWVTVYYGV: 84%

HXB2 Location gp160 (33–42)
Author Location Env (32–41 subtype B)
Epitope KLWVTVYYGV
Subtype B
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human (A2.1)
Keywords binding affinity

References Kundu *et al.* 1998a

- Ten HIV-1 + HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity.
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.

HXB2 Location gp160 (34–42)
Author Location
Epitope LWVTVYYGV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Assay type cytokine production, proliferation, Tetramer binding, Intracellular cytokine staining, Chromium-release assay
References Dagarag *et al.* 2003

- Telomer length is short in the CD8+ T-cell compartment of HIV-1 infected people, indicating excessive CTL activation and premature senescense. Here human telomerase RT (hTERT) transduction of HIV-1-specific CTL was used to study the functional impact of telomerase. Telomerase expression enhanced proliferative capacity, as well as cytolytic and antiviral capabilities; cytokine production was unchanged. hTERT transduced CTLs were 10-fold more efficient in controlling HIV-1 replication in culture. Thus telomerase transduction can restore CTL mediated cytolysis, and may have therapeutic potential.
- Three polyclonal CD8+ T-cell lines derived from an HIV-1, HLA A*0201 positive patient were used in this study, including one specific for this epitope.

HXB2 Location gp160 (34–55)
Author Location gp120 (25–46 BRU)
Epitope LWVTVYYGVPVWKEATTTLFCA
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dadaglio *et al.* 1991

- Defined through peptide blocking of CTL activity, and Env deletions.

HXB2 Location gp160 (36–44)
Author Location Env (35–)
Epitope VTVYYGVPV
Epitope name Env35
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Env *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human (A2)
Assay type CD4 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced a CD8+ T-cell IFN gamma response in 1/6 mice. Responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.

HXB2 Location gp160 (36–46)
Author Location Env
Epitope VTVYYGVPVWK
Epitope name Env 47
Subtype M
Immunogen Vaccine, in vitro stimulation or selection, computer prediction
Vector/Type: DNA, peptide *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, mouse (A*1101)
Assay type cytokine production, T-cell Elispot
Keywords inter-clade comparisons, computational epitope prediction, escape, TCR usage, variant cross-recognition or cross-neutralization
References McKinney *et al.* 2004

- This study examined variant recognition of epitopes presented by A*0201 and A*1101. Numerous amino acid substitutions can be introduced into epitopes without disrupting their recognition by CTLs, although epitopes with multiple substitutions were less recognized. An algorithm was constructed for prediction of epitopes capable of inducing responses to a great number of variant epitopes.
- A total of 9 variant forms of Env 47 were identified. More than 95% of the variant epitopes were recognized by CTLs from mice immunized with the parental form.
- Env 47 epitope (parent or variant form) was present in 82% of HIV sequences of many M group subtypes.

HXB2 Location gp160 (36–46)
Author Location gp120 (36–46 CM243 subtype CRF01)
Epitope VTVYYGVPVWR
Epitope name E36-4
Subtype CRF01_AE
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope after a second stimulation *in vitro* gave a weak response in HEPS study subject 186 who was HLA A2/A11.

HXB2 Location gp160 (36–46)

Author Location gp120 (36–46 CM243 subtype CRF01)
Epitope VTVYYGVPVWR
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This epitope was not predicted by the EpiMatrix method to be likely to bind to A11, though it served as an epitope in the FSWs, and it was one of the six A11 epitopes that had been previously defined.
- 1/8 tested FSWs recognized this epitope.
- This epitope was only conserved in CRF01 and subtypes B and C, and exact matches were uncommon.

HXB2 Location gp160 (36–46)
Author Location gp120
Epitope VTVYYGVPVWK
Immunogen HIV-1 infection
Species (MHC) human (A11, A*6801)
References Threlkeld *et al.* 1997

- Study of the fine specificity of an A3-like-HLA-super-type epitope (the A3-super-type includes A*0301, A*1101, A*3101, A*3301, and A*6801)
- The A3 super-type is characterized as a hydrophobic or hydroxyl containing anchor residue at position 2, and a positive charge in the C-term position.
- While most lines were specific, a promiscuous cloned CTL line was derived from an HIV+ donor that could recognize this epitope presented by either A11 or A*6801.

HXB2 Location gp160 (37–46)
Author Location gp120 (37–46 LAI)
Epitope TVYYGVPVWK
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (A*0301)
References Johnson *et al.* 1994b

- Multiple CTL clones obtained from two vaccinees.
- C. Brander notes that this is an A*0301 epitope in the 1999 database.

HXB2 Location gp160 (37–46)
Author Location gp120 (37–46 LAI)
Epitope TVYYGVPVWK
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (A*0301)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0301 epitope.

HXB2 Location gp160 (37–46)
Author Location gp120 (37–46 LAI)
Epitope TVYYGVPVWK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location gp160 (37–46)
Author Location gp120
Epitope TVYYGVPVWK
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human (A*0301)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used

in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location gp160 (37–46)
Author Location Env
Epitope TVYYGVPVWK
Immunogen Vaccine
Vector/Type: DNA
Species (MHC) transgenic mouse (A11)
References Ishioka *et al.* 1999
- A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed.
- The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans.
- HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes.

HXB2 Location gp160 (37–46)
Author Location Env
Epitope TVYYGVPVWK
Epitope name 1283
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A11, A2, A3, A6801, B18)
Donor MHC A25, A68, B18, B27; A03, A11, B14, B51, Cw08, Cw13
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003
- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for TVYYGVPVWK:18% Promiscuous epitope binding to A02, A03, A11, A6801 and B18.

HXB2 Location gp160 (37–46)
Author Location gp120 (37–46)
Epitope TVYYGVPVWK
Immunogen Vaccine
Vector/Type: canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease
Species (MHC) human (A3)
References Carruth *et al.* 1999
- The vaccine used was a live recombinant canarypox (CP) virus vaccine containing multiple HIV-1 genes (HIV-1 MN gp120, HIV-1 LAI gp41, HIV-1 LAI Gag, HIV-1 LAI protease)
- CD4+ and CD8+ Gag and Env specific CTL responses were detected in only 1/5 vaccinated volunteers, and were not detectable 1 year after vaccination.
- CTL responses to epitopes SLYNTVATL and TVYYGVPVWK from HIV+ control patients were used as positive controls.
- The study explored why vaccinees were non-responsive – non-response was not due to inherent defects or differences in the ability of these individuals to process and present antigen.

HXB2 Location gp160 (37–46)
Author Location gp120 (37–46 LAI)
Epitope TVYYGVPVWK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords review, escape
References Goulder *et al.* 1997e; Goulder *et al.* 1997a
- HLA-identical sibling hemophiliac brothers were both infected with the same batch of factor VIII.
- One had a response to this epitope, the other did not. They were tested 6-8 years after infection.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location gp160 (37–46)
Author Location gp120 (36–45)
Epitope TVYYGVPVWK
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Ferrari *et al.* 2000
- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location gp160 (37–46)
Author Location gp120 (37–46)
Epitope TVYYGVPVWK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords rate of progression, acute infection
References Day *et al.* 2001
- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.

HXB2 Location gp160 (37–46)
Author Location
Epitope TVYYGVPVWK

Epitope name Env-VK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A03, 0/20 (0%) recognized this epitope.

HXB2 Location gp160 (37–46)
Author Location gp160 (37–46)
Epitope TVYYGVPVWK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location gp160 (37–46)
Author Location gp120
Epitope TVYYGVPVWK
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A3)
Donor MHC A01, A03, B39, B44, Cw4, Cw6
Assay type T-cell Elispot
Keywords HIV exposed persistently seronegative (HEPS)
References Missale *et al.* 2004

- HIV-specific T-cell response was tested in HIV-uninfected patients exposed to blood from a patient with highly replicating HIV; these same patients were nosocomially infected with HBV. HIV-specific T-cell responses were directed to structural and non-structural HIV proteins in two patients suggesting that the virus replicated in these patients sufficiently to prime a cell-mediated immune response that protected these individuals from HIV infection.
- This patient responded to 3/11 HIV epitopes tested in an IFNgamma EliSpot assay. Responses were detected 16 and 20 weeks after exposure, but were lost by week 80.

HXB2 Location gp160 (37–46)
Author Location Env (49–58)
Epitope TVYYGVPVWK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location gp160 (37–46)
Author Location gp120 (38–41 LAI)
Epitope TVYYGVPVWK
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (A3.1)
References Johnson *et al.* 1994a

- Highly conserved epitope recognized by multiple CTL clones from vaccinee.

HXB2 Location gp160 (37–46)
Author Location gp120 (37–46 LAI)
Epitope TVYYGVPVWK
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (A3.1)
References Ferris *et al.* 1999; Hammond *et al.* 1995

- This peptide can be processed for HLA-A3.1 presentation by TAP-1/2 independent and dependent pathways.

HXB2 Location gp160 (38–48)
Author Location gp120 (45–55)
Epitope VYYGVPVWKEA
Immunogen HIV-1 infection
Species (MHC) human (Cw7)
References Nehete *et al.* 1998a

- Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one.
- HLA-C antigens are expressed on lymphoid cells to a lesser extent than either HLA-A or -B.
- HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing.

HXB2 Location gp160 (42–51)
Author Location gp120 (42–51 PV22)

Epitope VPVWKEATTT
Immunogen HIV-1 infection
Species (MHC) human (B*5501)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*5501 epitope.

HXB2 Location gp160 (42–51)
Author Location gp120 (42–51 PV22)
Epitope VPVWKEATTT
Immunogen HIV-1 infection
Species (MHC) human (B55)
References Brander & Walker 1995
- P. Johnson, unpublished.

HXB2 Location gp160 (42–51)
Author Location gp120 (41–55)
Epitope VPVWKEATTT
Immunogen HIV-1 infection
Species (MHC) human (B55)
References Ferrari *et al.* 2000
- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location gp160 (42–52)
Author Location Env (43–52 BH10, LAI)
Epitope VPVWKEATTTL
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002
- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this peptide is PVWKEATTTL) has similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta-3) (CD61): PLYKEATSTF.

HXB2 Location gp160 (42–52)
Author Location gp120 (42–52)
Epitope VPVWKEATTTL
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*3501 epitope.

HXB2 Location gp160 (42–52)
Author Location (C consensus)
Epitope VPVWKEAKTTL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*5301)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004
- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location gp160 (42–52)
Author Location gp120 (42–52 PV22)
Epitope VPVWKEATTTL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords inter-clade comparisons
References Cao *et al.* 1997a
- VPVWKEATTTL is the consensus sequence for clades B and D.
- VPVWKDAETTL is the consensus sequence for clade A and it is cross-reactive.
- VPVWKEADTTL is the consensus sequence for clade C and it is cross-reactive.
- VPVWKEADTTL is the consensus sequence for clade E and even with three substitutions still retains some cross-reactivity.

HXB2 Location gp160 (42–52)
Author Location gp120 (41–51)
Epitope VPVWKEATTTL
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Ferrari *et al.* 2000
- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location gp160 (42–52)
Author Location Env (41–50)
Epitope VPVWKEATTTL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004
- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 4/9 patients recognized this epitope.

HXB2 Location gp160 (42–61)
Author Location gp120 (49–68)

Epitope VPVWKEATTTLFCASDAKAY
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location gp160 (42–61)
Author Location gp120 (49–68 SF2)
Epitope VPVWKEATTTLFCASDAKAY
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- Three of these 11 had CTL response to this peptide.
- The responding subjects were HLA-A2, A3, B8, B62; HLA-A3, A24, B7, B38.

HXB2 Location gp160 (42–61)
Author Location gp120 (49–68 SF2)
Epitope VPVWKEATTTLFCASDAKAY
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location gp160 (42–61)
Author Location gp120 (11–30)
Epitope VPVWKEATTTLFCASDAKAY
Epitope name VPV
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This was one of 8 reactive peptides found not to vary over time. It was one of four epitopes that were not precisely defined.

HXB2 Location gp160 (50–59)
Author Location Env (62–71)
Epitope TTLFCASDAK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location gp160 (51–59)
Author Location Env (63–71)
Epitope TLFCASDAK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location gp160 (52–61)
Author Location gp120 (59–68 HXB2)
Epitope LFCASDAKAY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Lieberman *et al.* 1992

- CTL epitope defined by T cell line and peptide mapping.
- C. Brander notes that this is an A*2402 epitope in the 1999 database.

HXB2 Location gp160 (52–61)
Author Location gp120 (53–62 LAI)
Epitope LFCASDAKAY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*2402 epitope.

HXB2 Location gp160 (52–61)
Author Location gp120 (53–62)
Epitope LFCASDAKAY
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A24)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location gp160 (52–61)
Author Location gp120 (53–62)
Epitope LFCASDAKAY
Immunogen HIV-1 infection
Species (MHC) human (A24)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, T-cell Elispot, CD8 T-cell Elispot granzyme B
Keywords characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- Two of seven patients responded to this peptide with GzB producing cells, and a different patient with IFN-gamma producing cells.

HXB2 Location gp160 (52–61)
Author Location gp120 (53–62 LAI)
Epitope LFCASCAKAY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B38)
References Shankar *et al.* 1996

- Uncertain whether optimal, binds A24 as well.

HXB2 Location gp160 (52–71)
Author Location gp120 (59–78)
Epitope LFCASDAKAYDTEVHINVWAT
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location gp160 (52–71)
Author Location gp120 (59–78 SF2)
Epitope LFCASDAKAYDTEVHINVWAT
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-A2 and B-21.

HXB2 Location gp160 (62–80)
Author Location gp120 (69–88 SF2)
Epitope DTEVHNVWATHACVPTDPN
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-A2 and B-21.

HXB2 Location gp160 (67–75)
Author Location Env (67–)
Epitope NIWATHACV
Epitope name Env67(2I)
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* gp120 *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.
- The variant nVwathacv was also immunogenic in transgenic mice, but was not recognized in the 17 people tested.

HXB2 Location gp160 (75–84)
Author Location gp120
Epitope VPTDPNPPEV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type cytokine production, CD8 T-cell Elispot - IFNγ, Tetramer binding
References Höhn *et al.* 2003

- The M. tuberculosis HLA-A2 restricted epitope VLTDGNPPEV and this HLA-A2 HIV-1 gp120 VPTDPNPPEV epitope are cross-recognized. HLA-A2+ patients with pulmonary tuberculosis exhibit cross-reactivity with the HIV gp160 epitope, and those with HIV-1 infection have cross-reactive responses to M.tuberculosis antigen.

HXB2 Location gp160 (78–86)
Author Location gp120 (77–85)
Epitope DPNPQEVVL

Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Ogg *et al.* 1998b

- This epitope was included to illustrate the specificity of HIV-tetrameric staining, in a cross-sectional study correlating HLA A*0201 CTL effector cells and low viral load.

HXB2 Location gp160 (78–86)
Author Location gp120 (77–85 SF2)
Epitope DPNPQEVVL
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*3501 epitope.

HXB2 Location gp160 (78–86)
Author Location gp120 (77–85 SF2)
Epitope DPNPQEVVL
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 1997

- A CTL clone responsive to this epitope was obtained.
- 2/7 B35-positive individuals have a CTL response to this epitope.
- This epitope is highly variable.
- The substitutions: 1N, 3S and 7I, 7L and 9M, 8I, 8K all abrogate specific CTL lysis, while only 8K reduces binding to B*3501.
- The substitution 8V to 8E does not reduce specific CTL activity.

HXB2 Location gp160 (78–86)
Author Location Env (77–85)
Epitope DPNPQEVVL
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords HAART, ART
References Ogg *et al.* 1999

- CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SYLVANTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient.
- Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy.
- After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days.

HXB2 Location gp160 (78–86)
Author Location Env (77–85)
Epitope DPNPQEVVL
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Dyer *et al.* 1999

- CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective.
- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.

HXB2 Location gp160 (78–86)
Author Location
Epitope DPNPQEVVL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T cells and viral load.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location gp160 (78–86)
Author Location (SF2)
Epitope DPNPQEVVL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords rate of progression
References Kawana *et al.* 1999

- HLA B35 is associated with rapid disease progression.
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals.
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation.

HXB2 Location gp160 (78–86)
Author Location gp120 (77–85 SF2)
Epitope DPNPQEVVL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.

- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3.

HXB2 Location gp160 (78–86)
Author Location
Epitope DPNPQEVVL
Epitope name Env-DL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B35, 3/20 (15%) recognized this epitope.

HXB2 Location gp160 (78–86)
Author Location gp120 (78–86)
Epitope DPNPQEVVL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Donor MHC A3, A33, B14, B35, Cw*0401, Cw*0802
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location gp160 (78–86)
Author Location (C consensus)
Epitope DPNPQEMVL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location gp160 (78–86)
Author Location gp120 (47–55)
Epitope DPNPQEVAL
Epitope name DPN
Immunogen HIV-1 infection
Species (MHC) human (B35)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, immunodominance, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This epitope was one of six epitopes found to be under positive selection for escape mutations, and was mostly replaced by an escape variant between days 66 and 369 (dpnpqeAal)and,then replaced by a new escape variant (dpnpqevPl) by day 635.

HXB2 Location gp160 (78–86)
Author Location gp120 (77–85 SF2)
Epitope DPNPQEVVL
Immunogen HIV-1 infection
Species (MHC) human (B35, B51)
References Shiga *et al.* 1996

- Binds HLA-B*3501 and B*5101 – binds and kills gp120-vaccinia virus infected cells carrying B35 or B51.

HXB2 Location gp160 (78–86)
Author Location gp120 (77–85)
Epitope DPNPQEVVL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B51)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location gp160 (78–86)
Author Location gp160 (78–86)
Epitope DPNPQEVVL
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location gp160 (89–98)
Author Location Env
Epitope VTENFNMWKN
Epitope name 1284
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A11, A68, supertype)
Donor MHC A01, A68, B15, B40, Cw03; A03, A11, B14, B51, Cw08, Cw13
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, supertype, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for VTENFNMWKN:17%. This epitope can be presented by the A11, A68 supertype.

HXB2 Location gp160 (103–111)
Author Location Env (102–110)
Epitope QMHEDIISL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity, TCR usage
References Kmieciak *et al.* 1998a

- CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues.
- The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*.
- Peptides 4.3 and D1 bound HLA-A*0201 molecules with high affinity.
- Peptides 4.3 and D1 stimulated CTL with a relatively limited TCR Vβ repertoire.

HXB2 Location gp160 (104–112)
Author Location gp160 (104–112)
Epitope MHEDIISLW
Immunogen HIV-1 infection
Species (MHC) human (B*3801)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (104–112)
Author Location gp120 (104–112)
Epitope MHEDIISLW
Immunogen HIV-1 infection
Species (MHC) human (B*3801)
Donor MHC A3, A26, B7, B*3801, Cw*0702, Cw*1203
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.

- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location gp160 (104–119)
Author Location gp120 (111–126 IIIB)
Epitope MQEDIISLWDQSLKPC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Macatonia *et al.* 1991

- Primary CTL response with cells from non-infected donors stimulated by the peptide.

HXB2 Location gp160 (105–117)
Author Location gp120 (MN)
Epitope HEDIISLWDQSLK
Immunogen HIV-1 infection
Species (MHC) chimpanzee
References Lubeck *et al.* 1997

- No epitope-specific CTL were detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant despite a response to peptides P18 and T1.
- Helper and cytotoxic T cells have been found to be stimulated by this peptide (T2)

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Immunogen HIV-1 exposed seronegative
Species (MHC) human
References Pinto *et al.* 1995

- CTL and T helper cell reactivity in healthcare workers exposed to HIV.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Clerici *et al.* 1991a

- Helper and cytotoxic T cells can be stimulated by this peptide (T2)

HXB2 Location gp160 (108–116)
Author Location Env (107–115 subtype B)
Epitope IISLWDQSL
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN
HIV component: gp160
Species (MHC) human (A2.1)
Keywords binding affinity
References Kundu *et al.* 1998a

- Ten HIV-1 + HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity.
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.

HXB2 Location gp160 (109–117)
Author Location Env (109–117 CM243 subtype CRF01)
Epitope ISLWDQSLK
Epitope name E109-117
Subtype CRF01_AE
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Bond *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11, and had been predicted to be a possible A11 epitope using Epimer in Bond *et al.* [2001]

HXB2 Location gp160 (110–118)
Author Location Env
Epitope SLWDQSLKP
Epitope name 1328
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A02, A03, B08, B51, Cw01, Cw07
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, immunodominance
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for SLWDQSLKP: 50%.Immunodominant epitope.

HXB2 Location gp160 (112–130)
Author Location gp120 (119–139 SF2)
Epitope WDQSLKPCVKLTPLCVSLK
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.

- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-A2 and B-21.

HXB2 Location gp160 (112–131)
Author Location gp120 (MN)
Epitope WDQSLKPCVKLTPLCVTLNC
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A2
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement, HAART, ART
References Chitnis *et al.* 2003

- 17 perinatally HIV-1 infected children (0.08-16 years) were evaluated for HLA-A2-restricted IFN-gamma CD8+ CTL responses against 4 immunodominant peptides that carry HLA-A2 epitopes. Two peptides were from gp120 (one at position 112, one from the V3 loop), and one each was from gp41 and Gag. 15/17 patients responded to the Gag peptide, 13/17 to the gp41 and the non-V3 gp120 peptides, and 11/17 responded to the V3 loop. 4 children recognized all 4 peptides.

HXB2 Location gp160 (117–126)
Author Location Env (72–81)
Epitope KPCVKLTPLC
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Jin *et al.* 2000b

- This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor.
- A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing.

HXB2 Location gp160 (117–126)
Author Location Env
Epitope KPCVKLTPLC
Epitope name 1295
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for KPCVKLTPLC: 27%. This epitope was previously reported but not confirmed in this study.

HXB2 Location gp160 (121–129)
Author Location Env (120–128)
Epitope KLTPLCVTL
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity, TCR usage
References Kmieciak *et al.* 1998a

- CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL—all have A2 anchor residues.
- The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*.
- Peptides 4.3 and D1 bound HLA-A*0201 molecules with high affinity.
- Peptides 4.3 and D1 stimulated CTL with a relatively limited TCR Vβ repertoire.
- In a longitudinal study, the CTL response to the variable D2 epitope diminished over time, while the response to the conserved epitope D1 stayed higher over time.

HXB2 Location gp160 (121–129)
Author Location Env (134–)
Epitope KLTPLCVTL
Epitope name Env-134
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- 2/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT.
- 0/12 acutely infected individuals recognized this epitope.
- KLTPLCVTL binds to four HLA-A2 supertype alleles: A*0201, A*0202, A*0203 and A*6802 (highest affinity).

HXB2 Location gp160 (121–129)
Author Location Env
Epitope KLTPLCVTL
Epitope name Env 134
Immunogen Vaccine, in vitro stimulation or selection, computer prediction
Vector/Type: DNA
Species (MHC) human, humanized mouse (A*0201)

Assay type cytokine production, T-cell Elispot
Keywords inter-clade comparisons, computational epitope prediction, escape, TCR usage, variant cross-recognition or cross-neutralization
References McKinney *et al.* 2004

- This study examined variant recognition of epitopes presented by A*0201 and A*1101. Numerous amino acid substitutions can be introduced into epitopes without disrupting their recognition by CTLs, although epitopes with multiple substitutions were less recognized. An algorithm was constructed for prediction of epitopes capable of inducing responses to a great number of variant epitopes.
- A total of 19 variant forms of Env 134 were identified of which 10 were recognized by CTLs from transgenic mice immunized with the parental form.
- Env 134 epitope was present in 80% of HIV sequences of diverse M group HIV-1 subtypes.

HXB2 Location gp160 (121–129)
Author Location gp120 (120–128 LAI)
Epitope KLTPLCVTL
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN
HIV component: gp160
Species (MHC) human (A2)
References Dupuis *et al.* 1995

- CTL from HLA-A2 positive subject react with this peptide.

HXB2 Location gp160 (121–129)
Author Location gp120 (120–128)
Epitope KLTPLCVTL
Immunogen Vaccine
Vector/Type: vaccinia
Species (MHC) human (A2)
References Woodberry *et al.* 1999

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice.
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- KLTPLCVTL was recognized by 3 of the patients.

HXB2 Location gp160 (121–129)
Author Location gp120 (120–128)
Epitope KLTPLCVTL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords dendritic cells
References Kundu *et al.* 1998b

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients.
- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated.
- KLTPLCVTL is a conserved HLA-A2 epitope included in this study – all six patients had this sequence as their HIV direct sequence, and a detectable CTL response.
- CTL demonstrated against peptide-coated target, epitope is naturally processed and enhancible with vaccine.

HXB2 Location gp160 (121–129)
Author Location gp120 (120–128)
Epitope KLTPLCVTL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Kmieciak *et al.* 1998b

- Increased CTL response to cells expressing a VV construct Δv3 mutant compared with a full-length env gene product.

HXB2 Location gp160 (121–129)
Author Location gp120 (121–129)
Epitope KLTPLCVSL
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
Keywords dendritic cells
References Zarling *et al.* 1999

- This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses.
- Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA.
- A weak response to KLTPLCVSL was stimulated using macrophages as the APC.
- No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.

HXB2 Location gp160 (121–129)
Author Location gp120 (120–128)
Epitope KTLPLCVTL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location gp160 (121–129)
Author Location gp120 (121–129 IIIB)
Epitope KLTPLCVTL
Epitope name D1
Subtype B
Immunogen Vaccine
Vector/Type: DNA, DNA with protein boost *Strain:* B clade IIIB *HIV component:* gp160, gp160ΔV3 *Adjuvant:* IL-12
Species (MHC) mouse (A2)
Keywords vaccine-specific epitope characteristics
References Kiszka *et al.* 2002

- Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV.
- Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.

HXB2 Location gp160 (121–129)
Author Location Env (121–)
Epitope KLTPLCVTL
Epitope name Env121
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This epitope was one of the previously identified HLA-A2 epitopes studied.
- 3/17 HIV-infected HLA-A2+ people recognized this epitope.

HXB2 Location gp160 (121–129)
Author Location Env (134–142)
Epitope KLTPLCVTL
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

HXB2 Location gp160 (121–129)
Author Location Env
Epitope KLTPLCVTL
Immunogen Vaccine
Vector/Type: DNA
Species (MHC) transgenic mouse (A2.1)
References Ishioka *et al.* 1999

- A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed.
- The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans.
- HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong responses were observed to all nine epitopes, and CTL memory persisted up to four months after a single injection.

HXB2 Location gp160 (121–129)
Author Location Env (120–128 subtype B)
Epitope KLTPLCVTL
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human (A2.1)
Keywords binding affinity
References Kundu *et al.* 1998a

- Ten HIV-1 + HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity.
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.

HXB2 Location gp160 (156–165)
Author Location Env (162–171 BH10, LAI)
Epitope NCSFNISTSI
Immunogen HIV-1 infection

Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is STSIRGKVQK) has similarity with the macrophage colony stimulating factor I receptor fragment SISIRLKVQK.

HXB2 Location gp160 (156–165)
Author Location gp120 (156–165)
Epitope NCSFNISTSI
Immunogen HIV-1 infection
Species (MHC) human (Cw*08)
Keywords epitope processing
References Ferris *et al.* 1999

- Recognized by CTL clone LWF A5, isolated from a lab worker exposed to HIV-1 in 1985.
- The processing of this epitope is TAP1/2-dependent, as are most Env epitopes, and it contains two N-linked glycosylation sites that are glycosylated in Env.
- Only peptide that has been deglycosylated, a process that changes asparagine (N) to aspartic acid (D) was recognized: the aspartic acid at position 5 was critical, position 1 could be either D or N.
- This peptide also contains a Cys involved in a disulfide linkage but reducing conditions did not effect recognition by CTL clone LWF A5.
- The HIV-1 Env epitopes are typically processed by a TAP1/2 dependent mechanism, which involves cotranslational translocation into the ER, glycosylation, export back into the cytosol, and deglycosylation for processing, and retransport into the ER for the association with class I molecules.
- The particular pathway of generating an epitope may have an impact on the presentation of that epitope, quantitatively as well as qualitatively.

HXB2 Location gp160 (156–165)
Author Location gp120 (156–165 IIIB)
Epitope NCSFNISTSI
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
References Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.
- NCSFNITTSI, a variant found in HIV-1 MN, was not recognized, thus this epitope was type-specific.
- NCSFNISTSI contains two potential N-linked glycosylation sites and cysteine residue, possibly related to the requirement for a high sensitizing dose of peptide for CTL activity.

HXB2 Location gp160 (188–207)
Author Location gp120 (193–212 BRU)
Epitope TTSYTLTSCNTSVITQACPK
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dadaglio *et al.* 1991

- Defined through blocking CTL activity, and Env deletions.

HXB2 Location gp160 (191–200)
Author Location gp120 (194–202 CM243 subtype CRF01)
Epitope YRLINCNTSV
Epitope name E191-200
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.

HXB2 Location gp160 (191–200)
Author Location gp120 (194–202 CM243 subtype CRF01)
Epitope YRLINCNTSV
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by four amino acids, KLTSCNTSV.
- This epitope was somewhat conserved in 4/8 subtypes: CRF01 (E), B, C, and D.

HXB2 Location gp160 (192–200)
Author Location gp120 (192–199)
Epitope KLTSCNTSV
Epitope name SL9
Immunogen HIV-1 infection
Species (MHC) human (A*02)
Keywords HAART, ART
References Rinaldo *et al.* 2000

- Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that persist after therapy and long periods of virus being below the level of detection.

HXB2 Location gp160 (192–200)
Author Location gp120 (192–199 HXB2R)
Epitope KLTSCNTSV
Immunogen HIV-1 infection
Species (MHC) human (A2)

References Brander *et al.* 1995

- Epitope predicted on HLA binding motif, and studied in the context of inclusion in a synthetic vaccine.

HXB2 Location gp160 (192–200)
Author Location gp120 (192–199)
Epitope KLTSCNTSV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART
References Huang *et al.* 2000

- The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed.
- Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT.

HXB2 Location gp160 (192–200)
Author Location gp120 (197–205)
Epitope TLTSCNTSV
Immunogen Peptide-HLA interaction
Species (MHC) human (A2)
References Garboczi *et al.* 1992

- Crystallization of HLA-A2 molecules complexed with antigenic peptides – refers to Dadaglio *et al.* 1991.

HXB2 Location gp160 (192–200)
Author Location gp120 (161–169)
Epitope ILRSCNTSV
Epitope name ILR
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This was one of 8 reactive epitopes found not to vary over time.

HXB2 Location gp160 (192–200)
Author Location gp120 (199–207)
Epitope TLTSCNTSV
Immunogen HIV-1 infection
Species (MHC) human (A2.1)
References Brander *et al.* 1996

- This epitope was recognized by PBMC from 6/14 HIV+ asymptomatic patients.
- This epitope was used along with pol CTL epitope ALQDSGLEV and a tetanus toxin T helper epitope for a synthetic vaccine.
- This vaccine failed to induce a CTL response, although a helper response was evident.

HXB2 Location gp160 (192–211)
Author Location gp120 (199–219 SF2)
Epitope SLTSCNTSVITQACPKVSFE
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-A2, -B21.

HXB2 Location gp160 (199–207)
Author Location Env (202–210)
Epitope SVITQACPK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords inter-clade comparisons, TCR usage
References Fukada *et al.* 2002

- Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals.
- SVITQACPK was found to elicit clade-specific responses in clade B (SVITQACPK is most common, sAitqacpk is most common variant in clade A, C and D) and clade E (saiKqacpk is most common). SVITQACPK was recognized by CTL from 3/5 B clade infected Japanese subjects, and aiKqacpk by CTL from 0/7 E clade infected Thai subjects, so this seems to be a B clade exclusive epitope.
- The binding of the three variant peptides to HLA A*1101 was comparable, implicating TCR interaction differences.

HXB2 Location gp160 (199–207)
Author Location gp160 (199–207)
Epitope SVITQACPK
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (201–225)
Author Location gp120 (201–225 LAI)
Epitope ITQACPKVSFEPIPHYCAPAGFAI
Subtype B
Immunogen Vaccine

Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (CD4+ CTL)
References Johnson *et al.* 1994b; Johnson *et al.* 1994a
- CD4+ CTL isolated from LAI IIIB gp160 vaccinees.

HXB2 Location gp160 (202–221)
Author Location gp120 (209–228)
Epitope TQACPKVSFEPIPIHYCAPA
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995
- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location gp160 (202–221)
Author Location gp120
Epitope TQACPKVSFEPIPIHYCAPA
Immunogen HIV-1 infection
Species (MHC) human
Keywords TCR usage
References Weekes *et al.* 1999b
- Peptide 740.18: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed the CD28 depleted cell population.
- HIV CTL responses to 3 Env and 2 Gag peptides were studied.
- The clonal composition of the TCR Vβ responses were studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.1.

HXB2 Location gp160 (202–221)
Author Location gp120
Epitope TQACPKVSFEPIPIHYCAPA
Immunogen HIV-1 infection
Species (MHC) human
References Weekes *et al.* 1999a
- Peptide 740.18: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations.

HXB2 Location gp160 (202–221)
Author Location gp120 (209–228 SF2)
Epitope TQACPKVSFEPIPIHYCAPA
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a
- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- One of these 11 had CTL response to this peptide.

HXB2 Location gp160 (202–221)
Author Location gp120 (209–228 SF2)
Epitope TQACPKVSFEPIPIHYCAPA
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b
- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location gp160 (207–216)
Author Location gp120 (subtype A)
Epitope KMTFEPIPIH
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (A29)
Keywords inter-clade comparisons
References Cao *et al.* 2000
- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D.
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.
- CTL derived from subtype A clade infection (patient SP 528), recognized the subtype A version of the peptide (KMSFEPIPIH), had a slightly reduced specific lysis using the B clade version of the peptide (KVSFEPIPIH), and no lysis using the D clade version of the epitope (KVTFEPIPIH)
- Patient SP 528 is HLA A1, A29, B57, B81, Bw4, Bw6.

HXB2 Location gp160 (208–216)
Author Location Env
Epitope VSFEPIPIH
Epitope name 1329
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A23, B49, B57, C?; A03, A24, B27, B57, Cw13, Cw18
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003
- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for VSFEPIPIH: 58%

HXB2 Location gp160 (208–217)
Author Location gp120 (subtype B)
Epitope VSFEPIPIHY
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A29)

References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location gp160 (208–217)
Author Location gp120 (263–272)
Epitope VSFEPIPIHY
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A29)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location gp160 (208–217)
Author Location gp120
Epitope VSFEPIPIHY
Immunogen HIV-1 infection
Species (MHC) human (A29)
Assay type Intracellular cytokine staining
Keywords immunodominance, genital and mucosal immunity
References Kaul *et al.* 2003

- Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher.
- The immunodominant response was to this epitope in the PBMC of 1/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).

HXB2 Location gp160 (208–219)
Author Location Env
Epitope VSFEPIPPHYCA
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords epitope processing
References Cao *et al.* 2002

- SP 511 is an A2 restricted CTL clone generated from a Ugandan subject that recognizes VSFEPIPPHYCA.
- CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.

HXB2 Location gp160 (209–217)
Author Location gp160 (207–215 BORI, WEAU)
Epitope SFEPIPIHY
Epitope name gp160 SY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2902)
Donor MHC A*2902, B*1402, C*0802; A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, acute infection, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined, WEAU and BORI, had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape. This epitope was recognized in both patients.
- The patient BORI had high viral loads and rapid CD4 decline. BORI mounted 8 detected responses. BORI did not control viral replication well, and escape mutations occurred early and in most epitopes, 6/7 that were precisely identified. The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- Four escape variants to the SFEPIPIHY epitope were found in the patient BORI. SFdPIPIHY came up first, at day 55 from onset of symptoms, and caused a reduced cytotoxic response. By day 218, two rare forms were found, SIEPIPIHf and SiEPIPIHf. By day 556, only tFEPIPIHY was found. The weakest response was detected in the double mutant,SiEPIPIHf, yet tFEPIPIHY was the form that persisted.
- In WEAU, a minor variant, SsEPIPIHY was present at day 41. The SIEPIPIHf variant first came up day 136, gave a reduced CTL response, and then came to be the dominant form. Other variants were SFEPIPInY and SFEPIPIdf.

HXB2 Location gp160 (209–217)
Author Location (LAI)
Epitope SFEPIPIHY
Subtype B
Immunogen
Species (MHC) (A29)
Keywords optimal epitope
References Altfeld 2000; Frahm *et al.* 2004

HXB2 Location gp160 (209–217)
Author Location gp120 (213–221 SF2)
Epitope SFEPIPIHY
Immunogen HIV-1 infection
Species (MHC) human (A29)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A29+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/0 group 2, and 0/0 group 3.

HXB2 Location gp160 (209–217)
Author Location gp120 (209–217)
Epitope SFEPIPIHY
Immunogen HIV-1 infection
Species (MHC) human (A29)
Donor MHC A*0201, A29, B58, B62, Cw*0301, Cw*1601; A*0201, A29, B44, B60, Cw3, Cw16
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- Two subjects recognized this epitope during primary infection, both in the context of A29.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location gp160 (209–217)
Author Location (C consensus)
Epitope SFDPIPIHY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A29)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location gp160 (209–217)
Author Location (B consensus)
Epitope SFEPIPIHY
Epitope name SY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A29)
Donor MHC A28, A29, B14, B44, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope

HXB2 Location gp160 (212–231)
Author Location gp120
Epitope PIPIHYCAPAGFAILKCNNK
Immunogen HIV-1 infection
Species (MHC) human
References Weekes *et al.* 1999a

- Peptide 740.19: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations.

HXB2 Location gp160 (212–231)
Author Location gp120 (219–238 HXB2)

Epitope PIPIHYCAPAGFAILKCNNK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1992

- CTL epitope defined by T cell line and peptide mapping.

HXB2 Location gp160 (212–231)
Author Location gp120 (219–238)
Epitope PIPIHYCAPAGFAILKCNNK
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location gp160 (212–231)
Author Location gp120
Epitope PIPIHYCAPAGFAILKCNNK
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords TCR usage
References Weekes *et al.* 1999b

- Peptide 740.19: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population.
- HIV CTL responses to 3 Env and 2 Gag peptides were studied.
- The clonal composition of the TCR Vβ responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.6.

HXB2 Location gp160 (212–231)
Author Location gp120
Epitope PIPIHYCAPAGFAILKCNNK
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Jin *et al.* 1998b

- Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction.
- Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAG-FAILKCNNK.

HXB2 Location gp160 (237–246)
Author Location Env
Epitope GPCKNVSTVQ
Immunogen
Species (MHC) human (B56)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay.
- GPCKNVSTVQ was newly defined as an epitope in this study, was shown to stimulate an ELISPOT response, and to bind to HLA-B7.

HXB2 Location gp160 (239–247)
Author Location gp160 (237–245 BORI)
Epitope CKNVSTVQC
Epitope name gp160 CC9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw*0802)
Donor MHC A*2902, B*1402, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient BORI had high viral loads and rapid CD4 decline. BORI mounted 8 detected responses. BORI did not control viral replication well, and escape mutations occurred early and in most epitopes, 6/7 that were precisely identified.
- Four variants of the CKNVSTVQC epitope were found in the patient BORI. CeNVSTVQC and cCeNVSTVhC came up first, at day 6 from onset of symptoms. The CeNVSTVQC form was the form that persisted, with a second rare variant present at day 35, CgNVSTVQC.These variants were not tested for their impact on escape.

HXB2 Location gp160 (239–247)
Author Location gp120 (241–249 LAI)
Epitope CTNVSTVQC
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
References Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.
- CTNVSTVQC contains a potential N-linked glycosylation site and cysteine residues, possibly related to a requirement for a high sensitizing dose of peptide for CTL activity.

HXB2 Location gp160 (242–261)
Author Location gp120 (249–268)

Epitope VSTVQCTHGIRPVVSTQLLL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location gp160 (242–261)
Author Location gp120 (249–268 SF2)
Epitope VSTVQCTHGIRPVVSTQLLL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-2, -B21.

HXB2 Location gp160 (242–261)
Author Location gp120 (249–268)
Epitope VSTVQCTHGIRPVVSTQLLL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location gp160 (252–260)
Author Location gp120 (255–263 SF2)
Epitope RPIVSTQLL
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 1997

- A CTL clone responsive to this epitope was obtained.
- Only 1/7 B35-positive individuals had a CTL response to this epitope.
- An I to V substitution at position 3 reduces specific lysis, but not binding to B*3501.
- A Q to H substitution at position 7 abrogates specific lysis, but not binding to B*3501.

HXB2 Location gp160 (252–260)
Author Location gp120 (255–263 SF2)
Epitope RPIVSTQLL
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Shiga *et al.* 1996

- Binds HLA-B*3501.

HXB2 Location gp160 (252–260)
Author Location (SF2)
Epitope RPIVSTQLL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords rate of progression
References Kawana *et al.* 1999

- HLA B35 is associated with rapid disease progression.
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals.
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation.

HXB2 Location gp160 (252–261)
Author Location Env
Epitope RPVVSTQLLL
Immunogen
Species (MHC) human (B7)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 of the predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay.
- RPVVSTQLLL was one of the 15, and had been previously identified as an HLA-B7 epitope, and was confirmed in this study.

HXB2 Location gp160 (252–261)
Author Location Env
Epitope KPVVSTQLLL
Epitope name 1298
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7, B8)
Donor MHC A01, A03, B07, B08, Cw03, Cw07; A29, A30, B08, B44, Cw07, Cw16
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for KPVVSTQLLL: 46% Promiscuous epitope binding to B08 and B07.

HXB2 Location gp160 (252–261)
Author Location Env
Epitope RPVVSTQLLL
Epitope name 1305
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (B7, B8)
Donor MHC A29, A30, B08, B44, Cw07, Cw16
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, supertype, computational epitope prediction, cross-presentation by different HLA

References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for RPVVSTQLLL: 41%. Supertype epitope, published B07, responses by B08 subject.

HXB2 Location gp160 (252–271)
Author Location Env (256–268 BH10, LAI)
Epitope RPVVSTQLLLNGSLAEEEVV
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is STQLLLNGSLAEE) has similarity with the lymphatic endothelium-specific hyaluronan receptor LYVE-1 fragment TTRLLVQGSLRAEE.

HXB2 Location gp160 (252–271)
Author Location gp120 (256–275 LAI)
Epitope RPVVSTQLLLNGSLAEEEVV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Shankar *et al.* 1996

HXB2 Location gp160 (291–307)
Author Location Env (292–301 BH10, LAI)
Epitope SVEINCTRPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is VEINCTRPNN) has similarity with the FasI receptor precursor (Apptosis-mediating surface antigen fas) (APO-1 antigen) (CD95 antigen) fragment VEINCTRQN.

HXB2 Location gp160 (291–307)
Author Location gp120 (295–312 BRU)
Epitope SVEINCTRPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dadaglio *et al.* 1991

- Defined through blocking CTL activity, and Env deletions.

HXB2 Location gp160 (291–307)
Author Location gp120 (291–307 IIIB)
Epitope SVEINCTRPNNNTRKRI
Subtype B
Immunogen Vaccine
Vector/Type: DNA, DNA with protein boost
Strain: B clade IIIB *HIV component:* gp160
Adjuvant: IL-12
Species (MHC) mouse (A2)
Keywords vaccine-specific epitope characteristics
References Kiszka *et al.* 2002

- Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV.
- Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.
- The most intense CTL responses to the intact gp160 vaccine were directed at three V3 peptides.

HXB2 Location gp160 (296–305)
Author Location Env
Epitope CTRPNNNTRK
Epitope name 1265
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3, A2)
Donor MHC A03, A23, B49, B57, C?
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction, cross-presentation by different HLA
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for CTRPNNNTRK: 51% Promiscuous epitope binding to A02 and A03.

HXB2 Location gp160 (297–322)
Author Location gp120 (297–322 IIIB)
Epitope TRPNNNTRKRIRIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: V3 *Adjuvant:* liposome
Species (MHC) mouse (H-2D^{d})
References Chang *et al.* 1999

- Induction of peptide-specific CTLs in BALB/c mice was dependent on immunization with peptide encapsulated liposomes containing MPL as adjuvant.
- T26K (26mer) elicited a stronger AB and CTL response than R15K (a V3 15mer, RIQRGPGRAFVTIGK)

HXB2 Location gp160 (297–330)
Author Location Env (303–335 BX08)
Epitope TRPNNNTRKSIHIGPGRAFYATGEIIGDIRQAH

Immunogen Vaccine
Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 6/10 reacted to this peptide.
- 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in five vaccinees.
- None of the 12 tested had an IgG response to gp120 or gp160 and vaccinees could be differentiated from HIV-1 seropositive individuals with a commercial HIV detection kit – no neutralizing antibodies were observed.

HXB2 Location gp160 (298–307)
Author Location gp120 (298–307)
Epitope RPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC) human (B*07)
Keywords epitope processing, TCR usage
References Ferris *et al.* 1999; Hammond *et al.* 1995

- The processing of this epitope is TAP1/2-dependent, as are most Env epitopes, and it contains an N-linked glycosylation site that is glycosylated in Env.
- Peptide that had been deglycosylated, a process that changes asparagine (N) to aspartic acid (D) (RPNDNTRKSI) was recognized a 100-fold more efficiently than either glycosylated or non-glycosylated RPNNNTRKSI.
- Position 5 is not involved with HLA B*07 binding, so is probably important for TCR recognition.
- HIV-1 Env epitopes are typically processed by a TAP1/2 dependent mechanism, which involves cotranslational translocation into the ER, glycosylation, export back into the cytosol, and deglycosylation for processing, and retransport into the ER for the association with class I molecules.
- The particular pathway of generating an epitope may have an impact on the presentation of that epitope, quantitatively as well as qualitatively.

HXB2 Location gp160 (298–307)
Author Location gp120 (302–312 HXB2)
Epitope RPNNNTRKSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0702 epitope.

HXB2 Location gp160 (298–307)
Author Location (C consensus)
Epitope RPNNNTRKSI
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*4201)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location gp160 (298–307)
Author Location gp120 (302–312 HXB2)
Epitope RPNNNTRKSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Safrit *et al.* 1994b

- CTL from two acute seroconversion cases.

HXB2 Location gp160 (298–307)
Author Location gp120 (302–312 HXB2)
Epitope RPNNNTRKSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Hammond *et al.* 1995

- Peptide processed by a TAP-1/2-dependent pathway only.
- CTL from an acute seroconverter.

HXB2 Location gp160 (298–307)
Author Location gp120 (302–312 HXB2)
Epitope RPNNNTRKSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Wolinsky *et al.* 1996

- Longitudinal study of epitope variation *in vivo*.

HXB2 Location gp160 (298–307)
Author Location gp120 (302–311 subtype B)
Epitope RPNNNTRKSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords inter-clade comparisons, immunodominance
References Wilson *et al.* 1998b

- The extent of CTL interclade cross-reactivity from CTL isolated from individuals newly infected with B clade virus was studied, and extensive cross-reactivity was observed.

- Two HLA B7 individuals had CTL response to B_LAI, A_92UG037 and C_92BR025 gp160, but were B clade strain MN non-responders – the authors note that the B7 epitope RPNNNTRKSI is immunodominant, conserved between the LAI and clade A and C strains, but is very divergent in MN (RPNYNKRKRI), and that this epitope might be dominating the specificity of the response in the HLA B7 individuals.

HXB2 Location gp160 (298–307)
Author Location gp120 (303–312 SF2)
Epitope RPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 1/3 group 2, and 1/1 group 3.

HXB2 Location gp160 (298–307)
Author Location gp120 (298–307)
Epitope RPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location gp160 (298–307)
Author Location gp120 (298–307)
Epitope RPNNNTRKSI
Epitope name B7-RI10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 4/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.

HXB2 Location gp160 (298–307)
Author Location gp120
Epitope RPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A2, A3, B7, Bw6
Keywords HAART, ART
References Appay *et al.* 2002

- Four HIV patients with prolonged clinically successful antiviral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

HXB2 Location gp160 (298–307)
Author Location gp160 (298–307)
Epitope RPNNNTRRGI
Epitope name B7-RI10 Env
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), escape, early treatment, superinfection
References Altfeld *et al.* 2002a

- An HIV+ individual given acute ARV and undergoing STI developed a strong CTL immune response, but despite this was shown to be superinfected with second B clade virus. Some epitope variants of the second infecting virus were resistant to the initial CTL response.

- The first infecting strain had the variant rpSnntrKSi, and the CTL response was higher to the second variant, RPNNNTRRGI.

HXB2 Location gp160 (298–307)
Author Location gp120
Epitope RPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- No one pre-seroconversion, 0/9 HLA A2+ infection-resistant men, and 0/4 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location gp160 (298–307)
Author Location Env (302–311)
Epitope RPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 3/7 patients recognized this epitope.

HXB2 Location gp160 (298–307)
Author Location gp120 (303–312 IIIB)
Epitope RPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC) human (B7?)
Keywords responses in children, mother-to-infant transmission
References Wilson *et al.* 1996

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.
- RPNNNTRKDI and RPNNNTRKGI, naturally occurring variants, were found in non-transmitting mother – ability to recognize these variants has not yet been determined.

HXB2 Location gp160 (299–319)
Author Location Env (299–319)
Epitope PNNNTRKSIRIGPGQTFYA
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location gp160 (303–322)
Author Location gp120
Epitope TRKSIHIGPGRAFYTTGE
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* B clade consensus *HIV component:* Gag, V3
Species (MHC) mouse
References Luo *et al.* 1998

- Intramuscular injection of chimeric gag-env virus-like particles (VLPs) containing V3 loop sequences into BALB/c mice induce V3 specific CTL – TRKSIHIGPGRAFYTTGE is a B subtype consensus that stimulated a cross-reactive CTL response.

HXB2 Location gp160 (304–318)
Author Location gp120 (304–318 IIIB)
Epitope RKSIRIQRGPGRAFV
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* B clade IIIB, B clade MN, B clade RF, B clade SF2, HIV-2 VLP *HIV component:* Gag, V3
Species (MHC) mouse (H-2^d)
References Kang *et al.* 1999

- Virus-like particles could be formed from HIV-2 gag after deleting 143 amino acids at the C-terminal end – a proline rich region in positions 373-377 was critical to VLP formation.
- CTL responses in BALB/c mice were induced by chimeric gag-V3 particles against the V3 region of HIV-1 clade B isolates IIIB (SIRIQRGRAFVTI), MN (KRIHIGPGRAFYTTK), RF (SITKGPGRVIYATGQ), and SF2 (SIYIGPGRAFHTTGR)
- The vaccine induced CTL were cross-reactive with a broad spectrum of B clade isolates, with the exception of the RF V3 which did not induce CTL.

HXB2 Location gp160 (305–321)
Author Location gp120 (MN)
Epitope KRIHIGPGRAFYTTK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A2
Assay type CD8 T-cell Elispot - IFNγ

Keywords assay standardization/improvement, HAART, ART
References Chitnis *et al.* 2003

- 17 perinatally HIV-1 infected children (0.08-16 years) were evaluated for HLA-A2-restricted IFN-gamma CD8+ CTL responses against 4 immunodominant peptides that carry HLA-A2 epitopes. Two peptides were from gp120 (one at position 112, one from the V3 loop), and one each was from gp41 and Gag. 15/17 patients responded to the Gag peptide, 13/17 to the gp41 and the non-V3 gp120 peptides, and 11/17 responded to the V3 loop. 4 children recognized all 4 peptides.

HXB2 Location gp160 (306–322)
Author Location gp160 (LAI)
Epitope SIRIQGPGRAFVTIGI
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160 *Adjuvant:* aluminum hydroxide, CpG immunostimulatory sequence (ISS)
Species (MHC) mouse (H-2D^{d})
Keywords immunodominance, Th1, Th2
References Deml *et al.* 1999

- Addition of CpG oligodeoxynucleotide to a gp160/alum vaccine given to BALB/c mice shifted the response to Th0/Th1 from Th2, but no still CTL response to this immunodominant epitope was induced.

HXB2 Location gp160 (308–321)
Author Location Env (gp160)
Epitope RIQRGPGRAFVTIK
Epitope name P18IIIB
Immunogen Vaccine
Vector/Type: hemagglutinating virus of Japan (HVJ)-liposome *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse
Donor MHC H-2d
Assay type cytokine production, Chromium-release assay
Keywords genital and mucosal immunity
References Sakaue *et al.* 2003

- BALB/c mice were immunized nasally with HIVgp160-encapsulated hemagglutininating virus of Japan (HVJ)-liposome. Vaccination induced IgG in serum and IgA in nasal wash, saliva, fecal extract, and vaginal wash, with some ability to neutralize the primary field isolate HIV-MNp.
- Th1 and Th2-type responses were stimulated, as well as gp160 V3-specific MHC class I-restricted CTL responses.

HXB2 Location gp160 (308–321)
Author Location Env (IIIB)
Epitope RIQRGPGRAFVTIG
Epitope name P18IIIB
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* V3
Species (MHC) mouse (Dd)
Keywords binding affinity, Th1
References Ahlers *et al.* 2001

- BALB/c and A.AL were immunized with an Env-peptide vaccine construct containing the CTL epitope P18IIIB and the T helper epitope T1, KQIINMWQEVGKAMYA.
- Substitution of Glu (wt) to Ala in T1, kqiinmwqAvgkamya, caused increased affinity for MHC class II Ek, resulting in the upregulation of CD40L in the responding Th cells, and shifting the response towards Th1. Increased Th responses stimulated DCs to produce higher levels of IL-12, and B7-1 and B7-2, and enhanced CTL responses to P18.
- The modified epitope, T1A, elicited stronger protection against increasing doses of viral challenge with vaccinia expressing HIV-1 IIIB gp120 compared to the wt epitope T1.

HXB2 Location gp160 (308–322)
Author Location gp160 (MN)
Epitope RIHIGPGRAFYTTKN
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN *HIV component:* V3 *Adjuvant:* Montanide (ISA 51)
Species (MHC) human
References Pinto *et al.* 1999

- Peptide P18: Eight HIV+ individuals were vaccinated with peptides containing specific T helper, CTL and Ab epitopes in Montanide ISA 51 in a Phase I trial.
- Four displayed a 4-fold increase in PCLUS 3-18 MN-specific T helper responses.
- One patient developed a new, sustained P18MN-peptide-specific CTL response – the patient's HLA haplotype was A2,30; B53,7; Cw2,4, and anti-HLA A2 antibody did not inhibit the response, suggesting it was not A2.
- Patients with low baseline Ab levels developed an increase of neutralizing Ab titers.
- No significant change was observed in plasma HIV viral loads and CD4 cell counts.

HXB2 Location gp160 (308–322)
Author Location gp120 (MN)
Epitope RIHIGPGRAFYTTKN
Immunogen HIV-1 infection
Species (MHC) chimpanzee
References Lubeck *et al.* 1997

- Epitope-specific CTL detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant.
- CTL response may account for protection against subsequent HIV-1 SF2 challenge in a chimpanzee lacking neutralizing antibodies.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen HIV-1 exposed seronegative
Species (MHC) human
References Pinto *et al.* 1995

- CTL and T helper cell reactivity in healthcare workers exposed to HIV.

HXB2 Location gp160 (308–322)
Author Location gp120 (313–327 MN)

Epitope RIHIGPGRAFYTTKN
Immunogen HIV-1 exposed seronegative
Species (MHC) human
References Pinto *et al.* 1995

- CTL and T helper cell reactivity in healthcare workers exposed to HIV.

HXB2 Location gp160 (308–322)
Author Location gp120 (110–122)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *Adjuvant:* FLt3 ligand (FL), GM-CSF, IL-12, IL-15, IL-2
Species (MHC) mouse
Keywords vaccine-specific epitope characteristics
References Moore *et al.* 2002a

- Intramuscular immunization of BALB/c mice with DNA vaccines carrying either gp160 or Nef in the expression vector plasmid pNGVL gave different responses – gp160 induced strong gp160-specific CTL and IFN-responses and low-titer humoral responses, and Nef generated humoral (IgG1, IgG2a) responses and IFN-responses but little CTL activity.
- Co-injection of DNA plasmids encoding cytokines and/or hematopoietic growth factors, IL2, IL-12, IL-15, Flt3 ligand (FL), and GMCSF tended to give responses that were enhanced quantitatively, but not altered qualitatively.
- Co-administration of GMCSF most strongly enhanced CTL and IFN-responses against pNGVL-gp160.
- Repeated immunization with pNGVL-Nef failed to induce CTL responses. Co-administration of IL-12 most strongly enhanced humoral and IFNgamma responses.
- FL, which enhances innate immune responses, in combination with IL-2, IL-12 or IL-15 generated with most potent Nef responses.

HXB2 Location gp160 (308–322)
Author Location gp140 (iiib)
Epitope RIQRGPGRAFTIGK
Subtype B
Immunogen Vaccine
Vector/Type: liposome, protein *Strain:* B clade IIIB *HIV component:* oligomeric gp140 *Adjuvant:* liposome
Species (MHC) mouse
Donor MHC H-2d
Assay type proliferation, Chromium-release assay
Keywords adjuvant comparison
References Richards *et al.* 2004

- Mice were immunized with gp140 and an adjuvant that was an oil-in -water emulsion containing liposomes with lipid A with encapsulated antigen. Stable and unstable emulsions were found to have similar potencies of inducing antigen-specific T-cell proliferation and IgG antibodies, but stable emulsions also induced antigen-specific CTL responses. Stable emulsions had lowered IgG2a/IgG1 ratios than unstable.

HXB2 Location gp160 (308–322)
Author Location Env (315–329)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Subtype B
Immunogen Vaccine
Vector/Type: DNA *HIV component:* HIV-1
Species (MHC) mouse (A*0201)
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance
References Singh *et al.* 2002; Sykes & Johnston 1999

- C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome.
- A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members.
- Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV (Pol), RIQRGPGRAFVTIGK (Env) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen.
- The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) human (A11)
References Achour *et al.* 1994

- One of 3 HLA type restrictions associated with this peptide.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 BRU)
Epitope RIQRGPGRAFVTIGK
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dadaglio *et al.* 1991

- Defined through blocking CTL activity, and Env deletions.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Clerici *et al.* 1991a

- Helper and cytotoxic T cells can be stimulated by this peptide (P18)

HXB2 Location gp160 (308–322)
Author Location gp120 (308–322 IIIB)
Epitope RIQRGPGRAFVTIGK
Subtype B
Immunogen Vaccine

Vector/Type: DNA, DNA with protein boost *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* IL-12
Species (MHC) mouse (A2)
Keywords vaccine-specific epitope characteristics
References Kiszka *et al.* 2002

- Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV.
- Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.
- The most intense CTL responses to the intact gp160 vaccine were directed at three V3 peptides.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (A2, A3)
References Achour *et al.* 1993

- Two of 3 HLA type restrictions associated with this peptide.

HXB2 Location gp160 (308–322)
Author Location gp160 (308–322)
Epitope RIQRGPGRAFVTIGK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* V3
Species (MHC) mouse (D^d)
References Takahashi *et al.* 1989a

- Positions R(8) and F(10) are important for MHC/peptide interaction.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* V3
Species (MHC) mouse (D^d)
References Sastry *et al.* 1992

- Free peptide injected into the footpad of a mouse could stimulate specific CTL.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN *HIV component:* V3
Species (MHC) mouse (D^d)
References Ahlers *et al.* 1997b

- PCLUS 3-18MN synthetic peptide vaccine construct contained T1 helper epitope covalently linked to truncated P18 CTL epitope.
- A substitution in the T1 peptide stimulated an enhanced Th response and class II binding specificity, which in turn enhanced CTL induction by vaccine.
- Construct PCLUS 3-18MN is currently in a phase I vaccine clinical trial.

HXB2 Location gp160 (308–322)
Author Location gp120 (313–327 MN)
Epitope RIHIGPGRAFYTTKN
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB, B clade MN *HIV component:* gp160
Species (MHC) mouse (D^d)
References Takahashi *et al.* 1989b

- Y(11 MN) exchange with V(11 IIIB) interchanges specificities.

HXB2 Location gp160 (308–322)
Author Location gp120 (313–327 IIIB, MN, RF)
Epitope SITKGPGRVIYATGQ
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade RF *HIV component:* gp160
Species (MHC) mouse (D^d)
References Takahashi *et al.* 1992

- Comparison of MN, IIIB, and RF specificities, position 11 is critical.

HXB2 Location gp160 (308–322)
Author Location gp160 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen in vitro stimulation or selection
Species (MHC) mouse (Dd)

Donor MHC H-2d
Keywords TCR usage
References Yokosuka *et al.* 2002

- The TCR repertoire and its specificity was studied through analyzing the spectrum of TCR-alpha and beta chains able to reconstitute a reaction to the H-2 Dd-restricted P18 peptide. The RT-1 TCR alpha chain was able to react with 1/3 of the tested TCR beta chains to create a specific response. Experiments in transgenic mice also supported the observation that a single TCR alpha chain would confer the specificity of the response and could interact with a large variety of TCR beta chains.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{d, p, u, q}$)
References Shirai *et al.* 1992; Shirai *et al.* 1993

- In a murine system multiple class I molecules can present this peptide, called P18, to CTL, including H-$2D^{d}$, H-$2D^{p}$, H-$2D^{q}$, H-$2L^{q}$
- The MHC class I molecule D^{d} as well as H-$2^{u,p,q}$, were found to present peptides P18 and HP53.
- The V-β usage in T cells showing cross-reaction between these two peptides was conserved for H-$2^{d,u,p}$, but not in H-2^{q}

HXB2 Location gp160 (308–322)
Author Location gp120 (HXB2)
Epitope RIQRGPGRAFVTIGK
Subtype B
Immunogen Vaccine
Vector/Type: protein *HIV component:* Gag, V3
Species (MHC) mouse (H-2^{d})
References Griffiths *et al.* 1993

- Gag-V3 fusion protein immunization elicited V3 CTL response in mice.

HXB2 Location gp160 (308–322)
Author Location gp120 (HXB2)
Epitope RIQRGPGRAFVTIGK
Subtype B
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* Env, Gag
Species (MHC) mouse (H-2^{d})
References Deml *et al.* 1997

- Env bound to virus-like particles (VLPs) can elicit a CTL response that is dependent on the amount of Env presented on the VLP.

HXB2 Location gp160 (308–322)
Author Location gp120 (313–327 MN)
Epitope RIHIGPGRAFYTTKN
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade MN *HIV component:* gp160, V3
Species (MHC) mouse (H-2^{d})
References Fomsgaard *et al.* 1998a

- Enhanced B and CTL responses to the V3 region occur following epidermal immunization by gene gun with a chimeric DNA vaccine of V3-hepatitis B surface antigen relative to a gp160 plasmid vaccine.

HXB2 Location gp160 (308–322)
Author Location gp120 (313–327 MN)
Epitope RIHIGPGRAFYTTKN
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN *HIV component:* V3 *Adjuvant:* GM-CSF, IL-12
Species (MHC) mouse (H-2^{d})
Keywords Th1
References Ahlers *et al.* 1996; Ahlers *et al.* 1997a

- Vaccine constructs containing helper, antibody and CTL peptide epitopes induce strong Th1, CTL and NAb responses against the autologous HIV-1 virus.
- The peptide CTL response was as cross-reactive as one elicited by a vaccinia construct expressing rgp160 MN.
- GM-CSF and IL-12 were the two cytokines most effective for inducing and boosting CTLs.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* B clade IIIB *HIV component:* Gag, V3
Species (MHC) mouse (H-2^{d})
References Layton *et al.* 1993

- V3-Ty-Virus-like particles can induce type-specific CTL in mice in the absence of adjuvant.

HXB2 Location gp160 (308–322)
Author Location gp120 (IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* IL-2, IL-2/Ig
Species (MHC) mouse (H-2^{d})
References Barouch *et al.* 1998

- A discistronic IL-2 gp120 expression vector gave a weaker CTL response than gp120 alone in the expression vector, however co-administration of an Il-2/IgG fusion protein enhanced the immune response and administration of a Il-2/IgG plasmid had a response that depended on the timing of administration.
- This study showed that a response to an HIV-1 DNA vaccine could be either augmented or suppressed by plasmid Cytokine/Ig administration.

HXB2 Location gp160 (308–322)
Author Location Env (308–322 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen Vaccine

Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* B7, CpG immunostimulatory sequence (ISS), in vivo electroporation
Species (MHC) mouse (H-2^{d})
Keywords Th1
References Uno-Furuta *et al.* 2001

- Peptide immunization usually doesn't elicit a good CTL response because epitopes are not internalized and processed and presented, so vaccination with electric pulsing was tried (i.m. injection followed by 8 electric pulses), to enhance peptide uptake through electroporation.
- BALB/c immunized with HIV P18 or hepatitis C P17 peptides with an electric pulse elicited a CTL response, those that did not receive the pulse did not.
- The CTL response was enhanced by addition of immunostimulatory sequences ISS in the plasmid pCMV-LacZ, that contains hexamers GACGTC, AGCGCT, AACGCT, sequences common in prokaryotic genomes but rare in eukaryotic genomes that elicit Th1 cytokines and result in B cell and T-cell proliferation.
- The CTL response was also enhanced by addition of B7-1 cDNA – the B7 family of proteins transduce co-stimulatory signals through interaction with CD28.

HXB2 Location gp160 (308–322)
Author Location gp160 (MN)
Epitope RIHIGPGRAFYTTKN
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade MN *HIV component:* gp160
Species (MHC) mouse (H-2^{d}, H-2^{b})
References Fomsgaard *et al.* 1998b

- CTL responses to a primary gene gun vaccination were rapid and strong for several methods of vaccinations: i.m., bupivacaine pretreatment, cardiotoxin pretreatment or gene gun – the CTL response was more rapid and consistent than the antibody response.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) mouse (H-2D$^{d, p, q}$, H-2^{u})
References Shirai *et al.* 1996b

- Multiple murine MHC can cross-present this epitope (P18) and HP53, DRVIEVVQGAYRAIR, to specific CTL.

HXB2 Location gp160 (308–322)
Author Location gp160 (IIIB)
Epitope GIHIGPGRAFYAARK
Immunogen Vaccine
Vector/Type: peptide, protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse (H-2D^{d})
Keywords Th1, Th2
References Morris *et al.* 2000

- LT(R192G) induces gp160-specific serum and mucosal IgG1 and IgG2a, systemic CTL activity and Th1 and Th2 cytokine responses upon internasal immunization.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* Cholera toxin (CT)
Species (MHC) mouse (H-2D^{d})
References Porgador *et al.* 1997

- A intranasal peptide vaccine with cholera toxin as a mucosal adjuvant was given.
- IIIB peptide referred to as R15K.
- Peptide-specific CTLs were induced after *in vitro* restimulation with peptide-pulsed targets.
- R15K was superior at inducing CTL compared to the RGPGRAFVTI, in contrast to the findings of Nehete *et al.*
- Memory CTL responses were induced.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: vaccinia with H1 influenza HA gene cassette *Strain:* B clade IIIB *HIV component:* p18 Gag
Species (MHC) (H-2D^{d})
References Chiba *et al.* 1999

- Vaccine was capable of priming P18IIIB specific CTL in BALB/c mice, but could not induce a P18IIIB-specific antibody response.

HXB2 Location gp160 (308–322)
Author Location gp120 (multiple)
Epitope RIHIGPGRAFYTTKN
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN, B clade SC *HIV component:* V3
Species (MHC) mouse (H-2D^{d})
References Casement *et al.* 1995

- V3 peptides from MN and SC induce murine CTL that are cross-reactive with diverse strains.

HXB2 Location gp160 (308–322)
Author Location gp120 (313–327 MN)
Epitope RIHIGPGRAFYTTKN
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* QS21
Species (MHC) mouse (H-2D^{d})
References Newman *et al.* 1997

- MN vaccine induced CTL reactive with MN, IIIB and RF vaccinia-expressed Env, but not this peptide.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK

Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* QS21
Species (MHC) mouse (H-2D^d)
References Newman *et al.* 1997

- IIIB vaccine induced IIIB type-specific CTL to this peptide (P18), and an additional Env CTL response that was cross-reactive.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2D^d)
References Takahashi *et al.* 1988

- V3 loop CTL response in mice vaccinated with gp160.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329)
Epitope RIQRGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: liposome *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* oligomannose
Species (MHC) mouse (H-2D^d)
References Fukasawa *et al.* 1998

- The peptide RIQRGPGRAFVTIGK was incorporated into liposomes and given as a subcutaneous injection, which induces a MHC class I restricted CTL response in mice.
- Liposomes coated with oligomannose show no toxicity and can elicit a potent CTL response upon a single subcutaneous infection, while non-coated liposomes do not, suggesting that oligomannose may be a good adjuvant for CTL responses.

HXB2 Location gp160 (308–322)
Author Location
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Subtype B
Immunogen Vaccine
Vector/Type: fusion protein with anthrax delivery domain *HIV component:* V3 *Adjuvant:* B. anthracia lethal toxin LF component
Species (MHC) mouse (H-2D^d)
Keywords epitope processing, vaccine-specific epitope characteristics
References Lu *et al.* 2000a

- Bacillus anthrax lethal toxin (LFn)-HIV fusion proteins are candidate HIV vaccines that are safe in mice, and LFn-V3 region fusion proteins induce CD8 T cells in BALBc mice. LFn causes exogenous protein to be taken up and processed in a class I pathway. Expressed proteins from Gag p24 and nef fragments cloned into the LFn expression plasmid stimulate gag-specific CD4 proliferation and CTL responses in HIV-infected donor PBMCs *in vitro*.

HXB2 Location gp160 (308–322)
Author Location gp120 (V3) (MN)
Epitope RIHIGPGRAFYTTKN
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* Cholera toxin (CT), GM-CSF, IL-12, IL-18, IL-1α
Species (MHC) mouse (H-2D^d)
References Staats *et al.* 2001

- Cholera toxin (CT) is a potent adjuvant used in animal studies that is not safe in humans, so combinations of cytokins were used in nasal immunization of BALB/c mice V3 peptides to attempt to replace CT as a potent adjuvant.
- Peptide vaccine induced CTL activity was significantly increased by IL-1alpha , IL-18, and GMCSF given alone as adjuvant, but CT gave more potent CTL activity than any single cytokine.
- Combinations of cytokins could be more potent that CT as an adjuvant. The highest tetramer binding of H-2Dd peptide-specific PBMC after nasal immunization was observed with IL-1alpha plus IL-18 as adjuvant.
- Nasal immunization with HIV peptide in the presence of IL-1alpha, IL-12 and GM- CSF induced IFN-gamma-secreting cells in the cervical lymph node, the lung and the spleen, and was associated with upregulation of MHC class II and B7.1 on nonlymphocytes in NALT/nasal mucosal cells.
- Consistent results were obtained for the IIIB and the MN peptides.

HXB2 Location gp160 (308–322)
Author Location gp160 (315–329 MN)
Epitope RIHIGPGRAFYTTKN
Epitope name P18
Immunogen in vitro stimulation or selection
Species (MHC) mouse (H-2D^d)
Donor MHC H-2d
Keywords TCR usage
References Yokosuka *et al.* 2002

- The TCR repertoire and its specificity was studied through analyzing the spectrum of TCR-alpha and beta chains able to reconstitute a reaction to the H-2 Dd-restricted P18 peptide. The RT-1 TCR alpha chain was able to react with 1/3 of the tested TCR beta chains to create a specific response. Experiments in transgenic mice also supported the observation that a single TCR alpha chain would confer the specificity of the response and could interact with a large variety of TCR beta chains.

HXB2 Location gp160 (308–322)
Author Location Env (IIIB)
Epitope RIQRGPGRAFVTIGK
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* poly(I:C), lipopolysaccharide (LPS)
Species (MHC) mouse (H-2D^d)
Assay type Chromium-release assay
Keywords epitope processing, vaccine-induced epitopes, Th1, Th2, immunotherapy, adjuvant comparison
References Fujimoto *et al.* 2004

- When BALB/c mice were immunized with recombinant HIV-1 Env gp120 or Influenza HA protein together with polyriboinosinic polyribocytidylic acid (poly (I:C)), an epitope-specific CD8+ class I MHC-restricted CTL response was observed. This response was not observed when LPS was used as adjuvant instead of poly (I:C) indicating activation of cellular immunity by poly (I:C). In the presence of poly (I:C), immature DC presented processed external antigen in association with class I MHC.

HXB2 Location gp160 (309–317)
Author Location gp120 (310–318 SF2)
Epitope IYIGPGRAF
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 1/4 HIV-1 + people tested.
- IYIGPGRAF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – no specific CTL clones were obtained.

HXB2 Location gp160 (309–318)
Author Location gp120 (314–323 CM243 subtype CRF01)
Epitope ITVGPGQVFY
Epitope name E309-318
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was strongly reactive in HIV+ control study subject 184 who carried HLA-A11.

HXB2 Location gp160 (309–318)
Author Location gp120 (314–323 CM243 subtype CRF01)
Epitope ITVGPGQVFY
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it.
- This epitope was not conserved in other subtypes, and exact matches were rare.

HXB2 Location gp160 (310–318)
Author Location gp160 (313–321 WEAU)
Epitope TLGPGRVLY
Epitope name gp160 TY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- This was one of five reasonably strong responses in early infection in the patient WEAU, and the epitope sequence did not vary during the first year of the infection.

HXB2 Location gp160 (310–318)
Author Location
Epitope HIGPGRAFY
Epitope name Env-HY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Donor MHC A*3002 A*3201 B*4501 B*5301 Cw*0401 Cw*1202
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.

- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- This epitope was newly defined in this study.
- Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes YPLTFGWCY, Nef(135-143), HLA B*5301; AETFYVDGA, RT(437-445), HLA B*4501; and RSLYNTVATLY, p17(76-86), HLA A*3002.
- Among HIV+ individuals who carried HLA A30, 3/16 (19%) recognized this epitope.

HXB2 Location gp160 (310–318)
Author Location gp120 (310–318)
Epitope HIGPGRAFY
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (310–318)
Author Location
Epitope HIGPGRAFY
Epitope name Env-HY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A02, 6/29 (21%) recognized this epitope.

HXB2 Location gp160 (310–323)
Author Location gp120 (315–328 MN)
Epitope HIGPGRAFYTTKNI
Epitope name p97
Immunogen Vaccine
Vector/Type: canarypox prime with pseudovirion boost *Strain:* B clade IIIB, B clade MN *HIV component:* Gag, gp120, Protease
Species (MHC) mouse (H-2D^{d})
References Arp *et al.* 1999

- The vaccine vCP205, canarypox vector, MN gp120 + Gag/Pro IIIB, with a HIV-1 pseudovirion boost was given to mice;)
- HIV-1 pseudovirion boost enhanced the CTL to this epitope in immunized BALB/ c mice as measured by CTL lysis and IFN gamma production.

HXB2 Location gp160 (311–318)
Author Location (MN)
Epitope IGPGRAFY
Immunogen Vaccine
Vector/Type: B. abortus complex *Strain:* B clade MN *HIV component:* V3
Species (MHC) mouse (H-2D^{d})
References Golding *et al.* 2002a

- Intranasal immunization of B. abortus conjugated to V3 peptides induces mucosal IFN-gamma producing T-cell responses in BALB/c mice.

HXB2 Location gp160 (311–319)
Author Location gp120 (311–320 IIIB)
Epitope RGPGRAFVT
Subtype B
Immunogen Vaccine
Vector/Type: DNA, DNA with protein boost *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* IL-12
Species (MHC) mouse (A2)
Keywords vaccine-specific epitope characteristics
References Kiszka *et al.* 2002

- Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV.
- Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.
- The most intense CTL responses to the intact gp160 vaccine were directed at three V3 peptides.

HXB2 Location gp160 (311–319)
Author Location gp120 (312–320 SF2)
Epitope IGPGRAFHT
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade SF2 *HIV component:* gp120
Species (MHC) mouse (D^{d})
References Selby *et al.* 1997

- Murine CTL response to peptide observed after immunization with DNA plasmid containing HIV-1 (SF2) gp120 gene regulated by bacteriophage T7 promoter.
- CTL response required coadministration of rec vaccinia virus expressing T7 RNA polymerase or T7 RNA polymerase soluble protein.

HXB2 Location gp160 (311–319)
Author Location gp120 (SF2)
Epitope IGPGRAFHT
Immunogen Vaccine
Vector/Type: DNA prime with gp120 boost *Strain:* B clade SF2 *HIV component:* gp120
Species (MHC) mouse (H-2D^{d})
References Barnett *et al.* 1997

- CTL were induced by vaccine, and restimulated *in vitro* with V3 peptide.
- DNA vaccine with protein boost stimulated both CTL and antibodies.
- Strains SF2 (IGPGRAFHT), US4 (IGPGRAFYA), and CM235 (IGPGQVFYR) were tested.

HXB2 Location gp160 (311–319)

Author Location gp120 (312–320 SF2)
Epitope IGPGRAFHT
Subtype B
Immunogen Vaccine
Vector/Type: DNA, vaccinia *Strain:* B clade SF2 *HIV component:* Gag, gp120
Species (MHC) mouse (H-2D^{d})
Assay type Chromium-release assay
Keywords epitope processing, vaccine-induced epitopes
References Doe *et al.* 1996

- Spleen cells from mice with distinct MHC types were infused into HIV vaccinated scid mice, to study the antigen presenting cells used by CTL induced in intramuscular injections. Bone marrow derived cells are used for presenation, but DNA infection is not required for priming, rather APCs can present proteins synthesized in other host cells.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: DNA prime with peptide boost *Strain:* B clade IIIB *HIV component:* CD4BS, gp160, HPG30, V3
Species (MHC) macaque
References Okuda *et al.* 1997

- Murine BALB/c (H-2^{d}) and macaque both showed highest level of CTL vaccine response when a DNA vaccine was boosted with a peptide including four peptide subtypes of the V3 region, HPG-30 and a fragment of the CD4 binding region.

HXB2 Location gp160 (311–320)
Author Location gp120 (318–327)
Epitope RGPGRAFVTI
Immunogen HIV-1 infection
Species (MHC) human
References Kmieciak *et al.* 1998b

- Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length env gene product.
- This epitope doesn't have A2 anchors, but has features that confer promiscuous A2 binding, which may relate to the inhibitory effect seen in this paper.

HXB2 Location gp160 (311–320)
Author Location Env (IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* MIP-1α
Species (MHC) mouse
References Lu *et al.* 1999

- MIP-1alpha co-inoculation increased IgG1/IgG2a ratio T-helper type 1 response.
- A MIP-1 alpha expression plasmid increased the CTL response to this DNA vaccine, as well as the T help response, presumably by the MIP-1 alpha interacting with T lymphocytes and macrophages.

HXB2 Location gp160 (311–320)
Author Location
Epitope RGPGRAFVTI
Epitope name P18
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade BH10 *HIV component:* gp120 *Adjuvant:* GM-CSF
Species (MHC) mouse
References Barouch *et al.* 2002

- gp120 encoding DNA co-injected with a plasmid carrying GM-CSF gave meager CD4+ T-cell responses in BALB/c mice relative to the enhanced response to bicistronic gp120 and GM-CSF cloned into the same vector and expressed from the same promoter.
- Both mono and bicistronic DNA vaccines induced similar CTL responses directed against the H-2Dd restricted P18 peptide RGPGRAFTVTI in murine splenocytes despite the greatly enhanced proliferative responses.

HXB2 Location gp160 (311–320)
Author Location gp120 (313–322 BRU)
Epitope RGPGRAFVTI
Epitope name Pep 09
Subtype B, C
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade BRU *HIV component:* gp160, Rev, Tat
Species (MHC) mouse
Keywords inter-clade comparisons, Th1
References Arora & Seth 2001

- Plasmid DNA encoding gp160, tat, rev was given i.m. to immunize BALB/c mice.
- Vaccine-induced CTL activity produced a low degree of cell lysis of V3-peptide pulsed target cells, using a B (RGPGRAFVTI) or C (RIGGPGQTFYATG) clade V3 peptides. Th1 proliferative T-cell responses were observed, and weak Ab responses.

HXB2 Location gp160 (311–320)
Author Location Env (IIIB)
Epitope RGPGRAFVTI
Epitope name 10 Env
Subtype B
Immunogen Vaccine
Vector/Type: influenza prime with vaccinia boost *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse
Donor MHC H-2d
Assay type cytokine production, proliferation, CD8 T-cell Elispot - IFNγ
Keywords Th1, Th2, genital and mucosal immunity
References Gherardi *et al.* 2003

- Mice were intranasally primed with a recombinant influenza virus A vector that carries HIV-1 Env inserted into its hemagglutinin protein. Boosting was performed intranasally with either influenza-Env or intraperitoneally with two vaccinia virus recombinants expressing the Env protein, VVenv and MVAenv.

- Peritoneal heterologous immunization with VVenv induced a 60-fold higher CD8+ IFN-gamma T cell responses than homologous influenza prime-boost. The intraperitoneal MVAenv boost response was greater than the VVenv boost in the spleen and genital lymph nodes, while the VVenv response gave the highest boost with the intranasal route.
- Mice with increased CD8+-T-cell responses also had a higher Th1/Th2 ratio, indicated by the cytokine secretion profile and the IgG2a/IgG1 ratio.

HXB2 Location gp160 (311–320)
Author Location gp160
Epitope RGPGRAFVTI
Epitope name P18-I10
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia with H1 influenza HA gene cassette *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse
Assay type Chromium-release assay
Keywords genital and mucosal immunity
References Kuribayashi *et al.* 2004

- The intraepithelial compartment of the intestinal mucosa is shown to be a major site for preventing virus spread by thymus-derived CD8alphaß-positive Ag specific CTLs and CD8alpha,alpha+gamma,delta cells, which regulate virus spread in a P18-I10 vaccinia vector mouse infection model.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
References Alexander-Miller *et al.* 1996

- This epitope stimulates a CTL line derived from an HIV negative donor.
- This immunogenic peptide does not have the known binding motif for A2.1.
- The same optimal peptide for this human HLA-A2.1 epitope was observed for a murine H-2 D^d epitope.

HXB2 Location gp160 (311–320)
Author Location gp120 (311–320 IIIB)
Epitope RGPGRAFVTI
Immunogen
Species (MHC) human (A*0201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0201 epitope.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) human (A2)
References Achour *et al.* 1996

- Individual was immunized with rec vaccinia gp160 IIIB and boosted with purified gp160.
- Lysis only occurs with IIIB P18 peptide pulsed onto autologous targets; MN, RF, SIMI P18 peptides fail to stimulate CTL.
- Restimulating immune cells from gp160 IIIB vaccinees with MN, RF, or SIMI P18 did not enhance the MN, RF, or SIMI specific CTL response.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 SIMI)
Epitope MGPKRAFYAT
Immunogen Vaccine
Vector/Type: vaccinia prime with gp160 boost *Strain:* B clade SIMI *HIV component:* gp160
Species (MHC) human (A2)
References Achour *et al.* 1996

- Individual was immunized with rec vaccinia gp160 SIMI and boosted with purified recombinant gp160 SIMI.
- P18 MN and RF peptides were able to stimulate the HIV-specific CTL that arose in response to the SIMI vaccination, thus the P18 MN peptide (IGPGRAFYTT) and the P18 RF peptide (KGPGRVIYAT) could cross-react.
- The P18 IIIB peptide does not cross-react (RGPGRAFVTI in the epitope region)
- gp160 SIMI primed immune cells could generate a significantly broader specificity when stimulated with P18 MN or P18RF peptides, but not P18 IIIB.

HXB2 Location gp160 (311–320)
Author Location gp120 (311–320)
Epitope RGPGRAFVTI
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Epitope name LR25
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG
Species (MHC) mouse (A2.1)
Keywords binding affinity, vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2001

- The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01).
- The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.
- HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants.
- All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: V3
Species (MHC) mouse (D)
References Nehete *et al.* 1995

- RGPGRAFVTI was defined as the optimal peptide for vaccination, out of RIQRGPGRAFVTIGK.
- This peptide, in a carrier-free form in Freund's adjuvant, could stimulate Env specific CTL in BALB/c mice.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: V3
Species (MHC) mouse (D^d)
Keywords dendritic cells
References Takahashi *et al.* 1993

- Successful priming with vaccination of peptide pulsed splenic dendritic cells.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: V3
Species (MHC) mouse (D^d)
References Takahashi *et al.* 1996

- Exposure of CD8+ CTL to free peptide corresponding to the epitope results in strong inhibition of the CTL response to targets presensitized with the same peptide.
- The authors propose this is due to a "self-veto", where the CTL is inactivated by a CD8+ cell carrying the appropriate peptide-MHC complex.

HXB2 Location gp160 (311–320)
Author Location gp120 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) mouse ($H\text{-}2^{d,\,p,\,u}$)
References Shirai *et al.* 1997

- Three class I MHC, $H\text{-}2^{d,p,u}$, that differ in sequence and serology, cross-present this peptide to T cells of each of the other haplotypes.
- The amino acids R, F, and I are each critical for strong CTL activity with all three MHC molecules.

HXB2 Location gp160 (311–320)
Author Location gp160
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: vaccinia
Species (MHC) mouse ($H\text{-}2^{d17}$)
References Hanke *et al.* 1998a

- MVA is an attenuated vaccinia that can not replicate in mammalian cells – strings of CTL epitopes were delivered and expressed in a MVA DNA vector.
- INFγ and CTL activity were induced after a single vaccination.
- An MVA boost enhanced the response.

HXB2 Location gp160 (311–320)
Author Location gp160
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: DNA, vaccinia *HIV component:* Env *Adjuvant:* IL-12
Species (MHC) mouse ($H\text{-}2^{d}$)
References Gherardi *et al.* 2000

- Induction of HIV-1 specific CD8 gamma IFN secreting cells was enhanced when IL-12 and Env were given together in a prime, followed by a VV expressing Env boost.
- If IL-12 was also delivered as a boost from the viral vector, impairment of the IL-12 effects was noted, indicating that the vaccination schedule can be a critical parameter for success with DNA and vaccinia vectors used in combination with immunomodulators.
- The negative effect observed when IL-12 was delivered with the boost involved nitric oxide.

HXB2 Location gp160 (311–320)
Author Location Env
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB
HIV component: gp160, Rev *Adjuvant:* IL-12, IL-15, IL-2
Species (MHC) mouse ($H\text{-}2^{d}$)
Keywords Th1
References Xin *et al.* 1999

- A study of the DNA vaccine pCMV160IIIB/REV with IL-15 and IL-2 or IL-12 expression plasmids.
- Intranasal immunization of BALB/c mice with HIV DNA and IL-15 plasmid induced increased Th1 and CTL responses.
- Co-administration of IL-15 with IL-12 or IL-2 plasmids did not alter the effect of IL-15.

- Both the CTL (peptide pulsed targets) and DTH response (injection of peptide into footpad) to this peptide was monitored.
- The Ab response to NNTRKSIRIQRGPGRAFVTIGKIGN was monitored, and IL-15 co-administration resulted in a decrease in the IgG1/IgG2a ratio.

HXB2 Location gp160 (311–320)
Author Location Env
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: vaccinia, Sindbis *HIV component:* V3
Species (MHC) mouse (H-2^d)
References Villacres & Bergmann 1999

- HIV-1 epitope p18 was expressed in two different vaccine vectors and the CTL response was compared in BALB/c mice.
- Class I tetramer staining showed that up to 13% of the CD8+ splenocytes were p18 specific in the acute response using vaccinia, only 4% using Sindbis.
- vp18 had more gamma IFN secreting splenocytes and activated CD4+ and CD8+ T cells.
- The overall decline in CD8+ T cells in the transition into memory was 2-3 fold for both vectors.
- Sindbis virus recombinants induced protective memory cytotoxic T cells, although reduced quantitatively, without vaccinia associated inflamation and replication.

HXB2 Location gp160 (311–320)
Author Location Env (318–327)
Epitope RGPGRAFVTI
Immunogen
Species (MHC) mouse (H-2^d)
Keywords epitope processing, immunodominance
References Lopez *et al.* 2000

- A series of protease and proteasome inhibitors was used to identify elements of the processing pathway of this epitope, called p18, both from within Env and from within a chimeric hepatitis B protein which allows proper processing.
- Lactacystin, a proteasome inhibitor, partially inhibits endogenous processing of p18 epitope suggesting both a proteasome pathway and an additional pathway can be used.
- Both TAP dependent and TAP-independent pathways can be used.
- 1,10-phenanthrolin (metallopeptidases inhibitor) blocks epitope presentation demonstrating metalloproteinase processing in the Tap-dependent pathway.
- The Tap-independent pathway does not involve processing by metalloproteinases.
- This epitope is immunodominant in mice, and is presented by multiple human HLA alleles – it as been suggested that the high processing efficiency of this epitope might result in poor presentation of co-expressed epitopes.

HXB2 Location gp160 (311–320)
Author Location gp120
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: vaccinia
Species (MHC) mouse (H-2^d)
References Hanke *et al.* 1998a; Hanke *et al.* 1998b

- This murine epitope was incorporated into a vaccine of CTL epitopes expressed together including 20 HIV epitopes recognized by humans from 12 HLA types, one murine HIV epitope and three macaque HIV epitopes, delivered in a vaccinia virus Ankara (VVA) construct.
- The murine vaccination was more effective at generating CTL when given i.v. rather than i.m.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: peptide *HIV component:* CD4BS, HPG30, V3 *Adjuvant:* IL-12
Species (MHC) mouse (H-2^d)
References Hamajima *et al.* 1997

- B cell epitope HGP-30 also serves as a CTL epitope.
- Vaccine combined HGP-30, V3 loop peptide variants, and CD4 binding site peptide.
- IL-12 expression plasmid included with the vaccination enhanced the CTL response.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2^d)
Keywords Th1, Th2
References Arai *et al.* 2000

- Low-dosage 8 Br-cAMP given in combination with a DNA vaccine to BALB/c mice increased IgG and sIgA levels, and enhanced Th1, Th2 and CTL activity – the adjuvant activity may be mediated by activation of the CMV promotor in the DNA vaccine.

HXB2 Location gp160 (311–320)
Author Location gp120 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: fusion protein with anthrax delivery domain *HIV component:* gp120
Species (MHC) mouse (H-2^d)
References Goletz *et al.* 1997

- Anthrax lethal toxin can deliver proteins to the cytosol of eukaryotic cells.
- A fusion protein linking the delivery domain of the anthrax protein to gp120 achieved cellular uptake, and gp120 was processed allowing presentation of this V3 epitope to CTL *in vitro*.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Epitope name I-10
Immunogen in vitro stimulation or selection
Species (MHC) mouse (H-2^d)
References Takahashi *et al.* 2001

- Pre-incubation of HIV-1 (IIIB) gp160 specific CTL with peptide without APCs reduced cytolytic activity 3.5 fold and induced peptide concentration dependent IL-2 unresponsiveness that might be due to IL-2Rbeta down regulation.
- An enhanced cytolytic activity was observed by addition of anti-IFN-gamma, TNF-alpha or MIP-1beta to I-10 suppressed CTLs.

HXB2 Location gp160 (311–320)
Author Location gp160 (IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) mouse (H-2^d)
Keywords Th1, Th2
References Shirai *et al.* 2001

- Helicobacter pylori induces Th1 responses early, but predominantly Th2 responses later in infection (at 6 weeks) – differentiation of HIV-1 gp160 CD4+ help and CD8+ CTL effector cells in response to HIV gp160-vaccinia vaccination is impaired in BALB/c mice infected with H. pylori.

HXB2 Location gp160 (311–320)
Author Location gp120 (V3) (IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: influenza *Strain:* B clade IIIB
HIV component: V3
Species (MHC) mouse (H-2^d)
Assay type Intracellular cytokine staining, Chromium-release assay
Keywords genital and mucosal immunity, memory cells, vaccine antigen design
References Garulli *et al.* 2004

- BALB/c mice were transiently infected vaginally with a recombinant influenza virus expressing an HIV CTL V3 epitope. Infection was promoted by prior progesterone treatment. This vaccination induced long-term cellular T-cell responses in mice. Responses were induced at both local mucosal and systemic sites against both influenza and V3 epitopes. Intranasal vaccination also resulted in T-cell responses in distant mucosal tissues.

HXB2 Location gp160 (311–320)
Author Location Env (89.6)
Epitope IGPGRARYAR
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade 89.6
HIV component: gp160
Species (MHC) mouse (H-2D)
References Belyakov *et al.* 1998b

- Recombinant modified vaccinia virus Ankara (MVA), an attenuated vaccina which has lost the ability to replicate in mammalian cells, was used as the live vector for this vaccine study.
- A single intrarectal mucosal immunization resulted in long lasting mucosal CTL responses and production of proinflammatory cytokines in mucosal sites, indicating that MVA was as effective in inducing mucosal CTL as replicating recombinant vaccinia.

HXB2 Location gp160 (311–320)
Author Location Env (IIIB)
Epitope IGPGRARYAR
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: V3
Species (MHC) mouse (H-2D)
References Belyakov *et al.* 1998a

- HIV protection and mucosal CTL response was studied – an HIV peptide immunogen could protect against gp160 expressing vaccinia in a murine intrarectal challenge system in which neutralizing Abs did not play a role, demonstrating mucosal CTL at the site of exposure can be protective.

HXB2 Location gp160 (311–320)
Author Location gp120 (MN)
Epitope IGPGRAFYTT
Immunogen Vaccine
Vector/Type: B. abortus complex
Species (MHC) mouse (H-$2D^d$)
References Lapham *et al.* 1996

- B. abortus-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice.

HXB2 Location gp160 (311–320)
Author Location gp160 (IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: non-replicating adenovirus *Strain:* B clade IIIB *HIV component:* Env, Rev
Species (MHC) mouse (H-$2D^d$)
References Bruce *et al.* 1999

- A good HIV-1 Env immune response using non-replicating adenovirus vectors in BALB/c mice is dependent upon the presence of the stimulatory tat/rev 5'splice-donor site sequence and the presence of Rev.
- Administration of monocistronic RAd501 expressing env and RAd46 expressing rev resulted in a positive CTL response, but required two immunizations for a CTL response comparable to that induced by the bicistronic virus RAd142.
- Administration of RAd501 alone gave a low CTL response, but no humoral response, suggesting a lower level of antigen may be required to stimulate CTL.

HXB2 Location gp160 (311–320)
Author Location gp120 (MN)
Epitope IGPGRAFYTT
Immunogen Vaccine
Vector/Type: B. abortus complex
Species (MHC) mouse (H-$2D^d$)
References Lapham *et al.* 1996

- B. abortus-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Peptide-HLA interaction
Species (MHC) mouse (H-$2D^d$)

References Takeshita *et al.* 1995

- XGPXRXXXXI are critical for binding, consistent with H-2D^d motif XGPX(RKH)XXX(X)(LIF)

HXB2 Location gp160 (311–320)
Author Location Env
Epitope RGPGRAFTVTI
Immunogen Vaccine
Vector/Type: DNA *HIV component:* V3
Species (MHC) mouse (H-2D^d)
References Hanke & McMichael 1999; Hanke *et al.* 1999

- Vaccinated mice elicited a CTL response to a gene gun-delivered multiepitope vaccine to two epitopes studied that are known to elicit CTL in mice: SYIPSAEKI from Plasmodium berghei and RGPGRAFTVTI from HIV-1 Env.
- Different vaccination protocols were tested and it was found that a gene gun mediated delivery followed by an MVA boost was as good as i. m. immunization followed by a MVA boost – this is advantageous as gene gun delivery requires far less DNA than i.m. DNA priming.
- CTL activity was high (60% - 70% specific lysis at effector target) when vaccinated with a single gene gun immunization and an MVA boost, and improved with two gene gun vaccinations.

HXB2 Location gp160 (311–320)
Author Location Env (IIIB)
Epitope RGPGRAFVTI
Epitope name I-10
Immunogen in vitro stimulation or selection
Species (MHC) mouse (H-2D^d)
Keywords epitope processing, immunodominance
References Nakagawa *et al.* 2000

- The CTL line LINE-IIIB was generated by repetitive restimulation of BALB/c spleen cells with vSC-25, IIIB gp160-expressing vaccinia.
- RGPGRAFVTI represents the active minimal epitope within the previously described immunodominant epitope P18IIIB (RIQRGPGRAFVTIGK, gp160(308-322)
- External processing of P18IIIB results in the removal of the 2 C-terminal residues (GK) of I-10 by ACE (angiotensin-1-converting-enzyme) in sera to produce I-10, and this processing is essential for target cell presentation of RIQRGPGRAFVTIGK.

HXB2 Location gp160 (311–320)
Author Location Env (IIIB)
Epitope RGPGRAFVTI
Epitope name p18-I10
Immunogen Vaccine
Vector/Type: vaccinia, vesicular stomatitis virus (VSV) *Strain:* B clade HXB2, B clade IIIB *HIV component:* Env, Gag
Species (MHC) mouse (H-2D^d)
Keywords immunodominance
References Haglund *et al.* 2002a

- Different HIV strains were used for different regions: Env IIIB, Gag HXB2
- BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag, Env, or both, and compared to using rec Env and Gag in vaccinia virus (rVVs). The primary response was determined by cell lysis, cytokine production and tetramer staining.
- Primary CTL responses to the immunodominant Env (RGPGRAFVTI) epitope peaked 5-7 days after intraperitoneal vaccination with Env-rVSV, 40% of the CD8+ cells were tetramer positive, and this response was 6-fold higher than the response to Env-rVV.
- Vaccinating with GagEnv-rVSV carrying both Gag and Env allowed recognition of both HIV-1 proteins, but at reduced levels compared to either Gag-rVSV or Env-rVSV alone.
- Intranasal immunization with Env-rVSV yielded CTL responses that were strong but reduced compared to an intraperitoneal route.

HXB2 Location gp160 (311–320)
Author Location Env (IIIB)
Epitope RGPGRAFVTI
Epitope name p18-I10
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia, vesicular stomatitis virus (VSV) *Strain:* B clade HXB2 *HIV component:* Env, Gag
Species (MHC) mouse (H-2D^d)
Keywords immunodominance
References Haglund *et al.* 2002b

- Different HIV strains were used for different regions: Env IIIB, Gag HXB2
- BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag or Env, or both, and retention of memory responses and recall responses were studied by tetramer staining and IFN-gamma production.
- Seven months after vaccination with Env-rVSV, 6% of the CD8+ cells were tetramer positive for the immunodominant Env epitope; these cells had a memory phenotype, CD44-Hi positive.
- Env in rec vaccinia virus (Env-rVV) elicited a strong recall response, with up to 45% to the CD8+ T-cell population tetramer positive and activated (expressing CD62L-Lo), and capable of IFN-gamma production.
- A prime with Env-rVSV and heterologous boost of Env-rVV gave remarkably high levels of memory cells, with approximately 1/3 of the CD8+ splenocytes being Env specific memory cells 150 days after the boost.
- A Gag-rVSV or EnvGag-rVSV prime and with a heterologous Gag-rVV or EnvGag-rVV boost combination gave 40% tetramer positive CD8+ cells, but the fraction of IFN-gamma producing cells was only about 25%. Still the heterologous vector prime-boost combination showed a profound benefit.
- A HIV-1 protein rVSV prime, rVV boost was a more potent combination than a vector reversal of a rVV prime and rVSV boost.

HXB2 Location gp160 (311–320)
Author Location gp120 (V3) (IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine

Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* Cholera toxin (CT), GM-CSF, IL-12, IL-18, IL-1α
Species (MHC) mouse (H-2D^d)
References Staats *et al.* 2001

- Cholera toxin (CT) is a potent adjuvant used in animal studies that is not safe in humans, so combinations of cytokins were used in nasal immunization of BALB/c mice V3 peptides to attempt to replace CT as a potent adjuvant.
- Peptide vaccine induced CTL activity was significantly increased by IL-1alpha , IL-18, and GMCSF given alone as adjuvant, but CT gave more potent CTL activity than any single cytokine.
- Combinations of cytokins could be more potent that CT as an adjuvant. The highest tetramer binding of H-2Dd peptide-specific PBMC after nasal immunization was observed with IL-1alpha plus IL-18 as adjuvant.
- Nasal immunization with HIV peptide in the presence of IL-1alpha, IL-12 and GM- CSF induced IFN-gamma-secreting cells in the cervical lymph node, the lung and the spleen, and was associated with upregulation of MHC class II and B7.1 on nonlymphocytes in NALT/nasal mucosal cells.
- Consistent results were obtained for the IIIB and the MN peptides.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: DNA prime with vaccinia boost *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* beta-glucan lentinan, IL-2/Ig, liposome, PLG
Species (MHC) mouse (H-2D^d)
Keywords immunodominance
References Wierzbicki *et al.* 2002

- BALB/c mice were give an oral immunization with (PLG)-encapsulated plasmid DNA expressing gp160 and a boost of rec gp160 vaccinia vectors (rVV) with addition of murine IL-2/Ig plasmid or lentinan-associated liposomes. Lentinan increased CTL activity as measured by Cr-release assays against the immunodominant epitope RGPGRAFVTI, but didn't alter Ab responses. IL-2/Ig increased both type I and II activities, and increased Env specific CTL and Abs. Administration of liposomes and PLG microparticles with adjuvants facilitated gastrointestinal uptake.

HXB2 Location gp160 (311–320)
Author Location gp120 (LAI)
Epitope RGPGRAFVTI
Epitope name P18
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* Gag, gp120 *Adjuvant:* CpG immunostimulatory sequence (ISS)
Species (MHC) mouse (H-2D^d)
References Horner *et al.* 2001

- Immunostimulatory sequences (ISS), also known as CpG motifs, stimulate innate immunity and enhance vaccine-specific immune responses.
- Intranasal immunization (i.n.) of BALB/c mice was more effective than intradermal (i.d.), and immunization with a gp120-ISS conjugate was more potent than immunizing with gp120 and separate ISS molecule – increased IgG1, IgG2a, IFN-gamma, MIP1-alpha and MIP1-beta production was observed, and only i.n. immunization gave IgA responses.
- The highest mucosal CTL activity in both the Lamina Propria and the Peyer's Patch was observed following intranasal delivery with the gp120/ISS conjugate.
- Cytokine, chemokine and CTL responses following gp120/ISS conjugate vaccination were CD4+ T-cell independent; gp120 specific antibodies were dependent on helper T cells.

HXB2 Location gp160 (311–320)
Author Location gp160 (V3) (IIIB)
Epitope RGPGRAFVTI
Epitope name I10
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2D^d)
Keywords acute infection
References Takahashi *et al.* 2002

- During acute infection, high doses of virus result in "clonal exhaustion", a depletion of antigen specific T-cells.
- Recently stimulated CTL from BALB/c mice vaccinated with gp160-vaccinia showed a dose- and time-dependent induction of apoptosis when stimulated with antigenic peptide or H-2Dd/peptide tetramers.
- Restimulated CTL showed an upregulation of CD3-chain phosphorylation in comparison to cells stimulated with target cells, indicative of TCR-mediated apoptosis. Furthermore, apoptosis was inhibited by cyclosporin A and U0126, a mitogen activated kinase inhibitor specific for the ERK1/ERK2 MAPK kinase pathway, and a caspase 3 inhibitor.

HXB2 Location gp160 (311–320)
Author Location gp160 (V3) (MN)
Epitope IGPGRAFYAT
Epitope name MNT10
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2D^d)
Keywords acute infection
References Takahashi *et al.* 2002

- During acute infection, high doses of virus result in "clonal exhaustion", a depletion of antigen specific T-cells.
- Recently stimulated CTL from BALB/c mice vaccinated with gp160-vaccinia showed a dose- and time-dependent induction of apoptosis when stimulated with antigenic peptide or H-2Dd/peptide tetramers.
- Restimulated CTL showed an upregulation of CD3-chain phosphorylation in comparison to cells stimulated with target cells, indicative of TCR-mediated apoptosis. Furthermore, apoptosis was inhibited by cyclosporin A and U0126, a mitogen activated

kinase inhibitor specific for the ERK1/ERK2 MAPK kinase pathway, and a caspase 3 inhibitor.

HXB2 Location gp160 (311–320)
Author Location gp160 (V3) (HIV-IIIB)
Epitope RGPGRAFVTI
Epitope name P18-I10
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* IL-15, IL-2
Species (MHC) mouse (H-2D^d)
Donor MHC H-2d
Assay type cytokine production, Tetramer binding, Chromium-release assay
References Oh *et al.* 2003a

- IL-2 and IL-15 in vaccinia constructs were given with an HIV gp160 vaccinia vaccine to BALB/c mice. Both IL-2 and IL-15 induced strong and long-lasting antibody responses. Short-term CTL responses against HIV gp120 were enhanced by IL-2, but IL-15 enhanced both immediate CD8+ T cell responses and CD8+ T memory cells.

HXB2 Location gp160 (311–320)
Author Location gp160 (IIIB)
Epitope RGPGRAFVTI
Epitope name P18-I10
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* B7, ICAM, LFA-3
Species (MHC) mouse (H-2D^d)
Donor MHC H-2d
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Tetramer binding
References Oh *et al.* 2003b

- BALB/c mice were vaccinated with T-cell depleted splenocytes pulsed with peptides given in combination with immunostimulatory molecules B7, ICAM or LFA expressed in a recombinant pox virus. Increasing antigen gave an increased frequency of CD8+ T-cells, but the co-stimulatory molecules increased the avidity of the response.

HXB2 Location gp160 (311–320)
Author Location (89.6)
Epitope IGPGRAFYAR
Subtype B
Immunogen Vaccine
Vector/Type: DNA *HIV component:* gp120 *Adjuvant:* Flex, a dendric cell growth factor
Species (MHC) mouse (H-2D^d)
Donor MHC H-2d
Assay type Intracellular cytokine staining
Keywords dendritic cells
References Sailaja *et al.* 2003

- BALB/c mice were given a DNA vaccine that contained gp120 DNA covalently attached to the extracellular domain of the Fms-like tyrosine kinase receptor-3 ligand (FLex), a dendritic cell growth factor.
- Mice vaccinated i.m. with the FLex:gp120 chimeric gene gave a DC expansion similar to native Flex protein.
- gp120-specific stable CD8+ T-cell responses lasted 114 days after a prime/boost, and were observed in the presence and absence of Flex-DNA-induced dendritic cell (DC) expansion; strong Ab responses required DC expansion.

HXB2 Location gp160 (311–320)
Author Location gp120 (V3)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: herpes simplex virus type-1 (HSV-1) amplicon *HIV component:* gp120
Species (MHC) mouse (H-2D^d)
Donor MHC H-2d
Assay type Tetramer binding, JAM cytotoxicity assay
Keywords kinetics, memory cells
References Wang 2003

- Prime-boost combinations of gp120 combined with herpes simplex virus type-1 (HSV-1) amplicon particles, or gp120 in naked amplicon plasmid DNA, were compared in BLAB/c mice. Plasmid prime with particle boosts gave the strong primary (2 weeks) and memory responses (4 months).
- CD8+ T-cells reached their peak 8-28 days after the initial amplicon delivery.

HXB2 Location gp160 (311–320)
Author Location gp120 (V3)
Epitope RGPGRAFVTI
Epitope name P18-I10
Immunogen Vaccine
Vector/Type: peptide, vaccinia *Strain:* B clade 89.6, B clade IIIB *HIV component:* gp160ΔV3 *Adjuvant:* Cholera toxin (CT), E. coli mutant heat labile enterotoxin (LT-R72), Incomplete Freund's Adjuvant (IFA), CpG immunostimulatory sequence (ISS)
Species (MHC) mouse (H-2D^d)
Assay type Chromium-release assay, Flow cytometric CTL assay
Keywords dendritic cells, Th1, Th2, genital and mucosal immunity
References Belyakov *et al.* 2004

- Transcutaneous immunisation (TCI) of BALB/c mice induced adjuvant-dependent HIV-1 specific CTL responses in the spleen and the gut mucosa that resulted in protection against mucosal challenge against a recombinant vaccina virus carrying HIV-1 env. Activated DCs from skin were shown to migrate to immune-inductive sites in gut mucosa and to present antigen directly to resident lymphocytes.

HXB2 Location gp160 (311–320)
Author Location gp120 (V3)
Epitope RGPGRAFVTI
Subtype B
Immunogen Vaccine

Vector/Type: herpes simplex virus type-1 (HSV-1) amplicon *Strain:* B clade LAI, B clade MN *HIV component:* gp120
Species (MHC) mouse (H-2D^d)
Assay type CD8 T-cell Elispot - IFNγ, Tetramer binding, JAM cytotoxicity assay
Keywords vaccine antigen design
References Hocknell *et al.* 2002

- BALB/c mice were immunized with HSV amplicons containing HIV-1 gp120. Helper virus free HSV-1 amplicon particles are capable of inducing potent cytoxic CD8+ T-cell and humoral immune responses to the HIV-1 antigen in mice. Previous infection with wild-type HSV-1 reduces amplicon-induced cellular immune responses to HIV gp120 modestly (40-60%), but severally reduced B-cell responses. The route of vaccination impacted the nature and level of the responses (i.m., i.d., and i. p.).

HXB2 Location gp160 (311–320)
Author Location gp120
Epitope RGPGRAFVTI
Subtype B
Immunogen Vaccine
Vector/Type: DNA, polyepitope *Strain:* B clade MN *HIV component:* gp120, Protease, RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) humanized mouse (H-2D^d)
Assay type CD8 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance, immunotherapy
References Isaguliants *et al.* 2004

- Immunization of HLA-A*0201-transgenic mice with synthetic genes encoding clusters of human A*0201 CTL epitopes located at the sites of drug resistance mutations, induced RT-specific cellular responses indicating the immunogenicity of these constructs. This vaccine strategy may be a first step towards a therapeutic vaccine against drug-resistant strains. This epitope was included as a mouse marker for a CD8+ T-cell response.

HXB2 Location gp160 (311–320)
Author Location
Epitope RGPGRAFVTI
Epitope name R10I
Immunogen Vaccine
Vector/Type: DNA, virus-like particle (VLP), polyepitope *HIV component:* Gag, p24 Gag, V3
Species (MHC) mouse (H-2D^d)
Assay type cytokine production, Chromium-release assay
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance
References Wild *et al.* 2004

- A codon optimized gag DNA vaccine was compared to a myristylation defective gag and p24 alone, both of which lack signals for secretion from transfected cells. Gag-derived immunogens that were secreted as VLPs and those that remained intracellular (p24) each produced strong CTL responses, and neither the size of antigen nor cellular trafficking and localization significantly influenced the strength of humoral and cellular immune activation. The formation and release of VLPs was not essential for eliciting strong CTL. BALB/c mice were given the DNA vaccine by i.m. administration of plasmid DNA for the prime and boost.
- Linking the region encoding the V3 immunodominant epitope to the gag gene did not diminish the response to the Gag p24 eptiope A9I, but did enable a response to the V3 epitope.
- Minigenes were made incorporating just one epitope, minitopes, carrying one of three murine class I eptiopes linked to the Ad2-E3 protein-derived signal peptide to allow access of the epitope to the ER. Weak induction of cellular immune resposes was observed, in contrast to the complex polyprotein.

HXB2 Location gp160 (311–320)
Author Location Env (318–327)
Epitope RGPGRAFVTI
Epitope name R10I
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2D^d)
Donor MHC H-2D
Assay type Intracellular cytokine staining
Keywords vaccine antigen design
References Samino *et al.* 2004

- The endogenous processing of the HIV-1 envelope glycoprotein generates several different natural peptidic species presented by the H-2D molecule in infected cells, the 9-, 10-, and 11-mer peptides, GPGRAFVTI, RGPGRAFVTI, and QRGPGRAFVTI. CTL with the same antigenicity could recognize all three forms. The complexity of the binding peptides suggests naturally processed proteins could provide more variety as antigens, stimualting more robust and diverse CTL responses.

HXB2 Location gp160 (311–320)
Author Location p18 (IIIB)
Epitope RGPGRAFVTI
Subtype B
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* IL-12
Species (MHC) mouse (H-2D^d)
Donor MHC H-2D
Assay type cytokine production, proliferation, CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, memory cells, characterizing CD8+ T cell responses
References Seaman *et al.* 2004

- Delivery of plasmid IL-12 on day 10 after immunization of mice with an HIV-1 gp120 DNA vaccine resulted in expansion of gp120-specific CD8+ T-cells but had no effect on antigen-specific CD4+ T-cells and antibody responses. gp120-specific CD8+ T-cells were shown to primarly be effector memory and not central memory T-cells and did not expand following gp120 boost immunization.

HXB2 Location gp160 (311–320)
Author Location gp160 (318–327 IIIB)
Epitope RGPGRAFVTI
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* Env, Nef
Species (MHC) mouse (L^d)
References Tobery & Siliciano 1997

- An HIV-1 Env vaccine was targeted for rapid cytoplasmic degradation.
- The rapidly degraded form rapidly stimulated CTL to this peptide, faster than the normal vaccinia-env.
- The rapidly degraded form also stimulated greater specific CTL lysis and higher CTLp frequencies than normal Env.
- Similar results were obtained for a Nef protein designed for rapid degradation.

HXB2 Location gp160 (312–320)
Author Location gp120 (V3) (IIIB)
Epitope GPGRAFVTI
Subtype B
Immunogen Vaccine
Vector/Type: fowlpoxvirus *Strain:* B clade BRVA, B clade IIIB, B clade JY1, B clade LR150, B clade MN, B clade RF *HIV component:* V3
Species (MHC) mouse ($H\text{-}2^d$)
Keywords vaccine-specific epitope characteristics, immunodominance
References Vázquez Blomquist *et al.* 2002

- BALB/c mice were vaccinated with a polyepitope V3 vaccine in a fowlpoxvirus carrying concatonated 15 mer sections of the V3 loops of HIV-1 isolates LR150, JY1, RF , MN, BRVA and IIIB with 5-aa linkers between, fused to the N-term of p64K protein from Neisseria meningitidis.
- Intraperitoneal immunization elicited the strongest V3-specific IFN-gamma response in splenocytes, compared to intravenous and subcutaneous immunization. Intraperitoneal immunization conferred protection in a recombinant vaccinia virus challenge model.
- The immunodominant response was directed against the IIIB peptide (the IIIB immunizing peptide was SIRIQRGPGRAFVTI, the peptide used to probe the response by Elispot was GPGRAFVTI).
- Low CTL responses were also detected to the LR150 (SRGIRIGPGRAILAT) and RF (RKRITMGPGRVYYTT) peptides, no responses were detected to the JY1 (RQSTPIGLGQALYTT), BRVA (RKSITKGPGRVIYAT), or MN (RKRIHIGPGRAFYTT) peptides.

HXB2 Location gp160 (312–320)
Author Location gp120 (V3)
Epitope GPGRAFVTI
Subtype B
Immunogen Vaccine
Vector/Type: DNA prime with vaccinia boost, polyepitope, DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* B clade BRVA, B clade IIIB, B clade JY1, B clade LR150, B clade MN, B clade RF *HIV component:* V3 *Adjuvant:* IFNγ
Species (MHC) mouse ($H\text{-}2^d$)
Assay type cytokine production, CD8 T-cell Elispot - IFNγ
Keywords Th1
References Gómez *et al.* 2004

- Priming of mice with DNA-TAB vector, a polyepitope string carrying 8 different V3 loop sequences, followed by a booster with VV-TAB or MVA-TAB, induced humoral responses, as well as a CD8+ T-cell response against V3 epitopes from three different subtype B HIV isolates. The highest values of specific CD8+ T-cell response were achieved when priming with DNA-TAB and a DNA vector expressing IFN-gamma, followed by a MVA-TAB boost. The T-cell response was Th1.
- The eight V3 loops were linked with an A-G-G-G-A sequence. The three peptides that elicited a response were LR150, SRGIRIGPGRAIL; MN, RKRIHIGPGRAFY; and IIIB, SIRIQRGPGRAFVTI. These peptides were located at the beginning, middle and end of the polyepitope, indicating all parts were able to be processed. It is not known if there is an H-2d epitope in the other five V3 loop variants that did not elicit a response.

HXB2 Location gp160 (314–322)
Author Location gp120 (312–320)
Epitope GRAFVTIGK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*2705)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- One of seven patients responded to this peptide with GzB producing cells and with IFN-gamma producing cells.

HXB2 Location gp160 (314–322)
Author Location gp120 (314–322)
Epitope GRAFVTIGK
Immunogen Peptide-HLA interaction
Species (MHC) human (B27)
References Jardetzky *et al.* 1991

- Study of peptide binding to HLA-B27.

HXB2 Location gp160 (337–361)
Author Location gp120 (337–368 LAI)
Epitope KWNNTLKQIDSKLREQFGNNKTIIF
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (CD4+ CTL)
References Johnson *et al.* 1994a

- CD4+ CTL clones were obtained from an HIV-1 vaccinia-env vaccinee.

HXB2 Location gp160 (339–354)
Author Location gp120 (339–361 LAI)
Epitope NNTLKQIDSKLREQFG
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (CD4+ CTL)
References Johnson *et al.* 1994b

- CD4+ CTL isolated from LAI IIIB gp160 vaccinees.

HXB2 Location gp160 (340–348)
Author Location gp120 (346–354 CM243 subtype CRF01)
Epitope RVLKQVTEK
Epitope name E340-348
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was weakly reactive in HIV+ control study subject 053 who carried HLA-A11.

HXB2 Location gp160 (340–348)
Author Location gp120 (346–354 CM243 subtype CRF01)
Epitope RVLKQVTEK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it.
- This epitope was not conserved in other subtypes, and exact matches were rare.

HXB2 Location gp160 (340–349)
Author Location gp120 (W6.ID)
Epitope NTLKQIVIKL
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade W61D
HIV component: gp120
Species (MHC) chimpanzee (Patr-B*14)
Keywords immunodominance
References Balla-Jhagjhoorsingh *et al.* 1999a

- An HIV-1 rgp120 vaccine induced strong humoral and cellular immune response in sibling chimpanzees, but only one of the two made a detectable CTL response to this Patr-B*14 restricted immunodominant epitope.

HXB2 Location gp160 (344–361)
Author Location gp160 (348–366 WEAU)
Epitope QIVEKLREIKQFKNKTIVF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- WEAU had a reaction to an eptiope within this peptide, and there was very rapid accumulation of substitutions; variation continued through the last sample collected.

HXB2 Location gp160 (369–375)
Author Location gp120 (374–380 BRU)
Epitope PEIVTHS
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dadaglio *et al.* 1991

- Defined through blocking CTL activity, and Env deletions.

HXB2 Location gp160 (374–382)
Author Location Env
Epitope HSFNCGGEF
Epitope name 1325
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A3)

Donor MHC A02, A03, B08, B51, Cw01, Cw07
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for HSFNCGGEF: 76%

HXB2 Location gp160 (375–383)
Author Location gp120 (379–387 LAI)
Epitope SFNCGGEFF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1516)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*1516 epitope.

HXB2 Location gp160 (375–383)
Author Location gp120 (375–383 IIIB)
Epitope SFTCGGEFF
Immunogen HIV-1 infection
Species (MHC) human (B15)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- An additional variant that gave a positive, though reduced, CTL response: SSTCGGEFF and SFTCGGGFF.
- SFTCGGGVF was an escape mutant.

HXB2 Location gp160 (375–383)
Author Location gp120 (375–383 SF2)
Epitope SFNCGGEFF
Immunogen HIV-1 infection
Species (MHC) human (B15)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with preseroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B15+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/1 group 3.

HXB2 Location gp160 (375–383)
Author Location gp120 (375–383)
Epitope SFNCGGEFF
Immunogen HIV-1 infection
Species (MHC) human (B15)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 5 epitopes from this individual that varied over time where the internal mutations became fixed; a dramatic decrease in CTL activity against the wild type epitope was observed as the mutation arose. The sfncRgeff variant residue found at 20 and 47 months postseroconversion.

HXB2 Location gp160 (375–383)
Author Location gp120 (375–383 IIIB)
Epitope SFNCGGEFF
Immunogen HIV-1 infection
Species (MHC) human (B63, B15)
References Wilson *et al.* 1997a

- This is the optimal peptide for two CTL clones that recognize this epitope in the context of two different HLA molecules, Cw4 and B15.
- Predominant form in proviral DNA of the individual with B15 restricted CTL was SFTCGGEFF and this was recognized.
- Recognition of a minor autologous variant (SFNCRGEFF) from the B15 donor was greatly reduced.

HXB2 Location gp160 (375–383)
Author Location gp120 (376–383 PV22)
Epitope SFNCGGEFF
Immunogen HIV-1 infection
Species (MHC) human (Cw*0401)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a C*0401 epitope.

HXB2 Location gp160 (375–383)
Author Location gp120
Epitope SFNCGGEFF
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (Cw*0401, Cw*0407)
Keywords HIV exposed persistently seronegative (HEPS), cross-presentation by different HLA
References Bird *et al.* 2002

- 4/123 (2 HIV-1 positive, 2 HEPS) Kenyan female sex workers carried the novel allele HLA Cw*0407.
- HLA Cw*0407 did not differ from Cw*0401 in the region associated with the binding pocket, and Cw*0407 was shown to cross-present a previously defined Cw*0401 epitope, SFNCGGEFF (gp120).

HXB2 Location gp160 (375–383)
Author Location gp120 (376–383 PV22)
Epitope SFNCGGEFF
Immunogen HIV-1 infection
Species (MHC) human (Cw4)
References Johnson *et al.* 1993
- Conserved epitope.

HXB2 Location gp160 (375–383)
Author Location gp120 (376–383 PV22)
Epitope SFNCGGEFF
Immunogen HIV-1 infection
Species (MHC) human (Cw4)
References Wolinsky *et al.* 1996
- Longitudinal study of epitope variation *in vivo*.

HXB2 Location gp160 (375–383)
Author Location gp120 (376–383)
Epitope SFNCGGEFF
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (Cw4)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-Cw4 women, 1/2 HEPS and 10/11 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in 6 of the 10/11 responsive HIV-1 infected women, and not in the HEPS case.

HXB2 Location gp160 (375–384)
Author Location (B consensus)
Epitope SFNCGGEFFY
Epitope name SY10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A29)
Donor MHC A28, A29, B14, B44, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c
- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location gp160 (376–383)
Author Location gp120
Epitope FNCGGEFF
Immunogen
Species (MHC) human (Cw4)
References Rowland-Jones *et al.* 1999
- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive,
- HIV-2 sequence: TNCRGEFL – no cross-reactivity Johnson *et al.* [1993]

HXB2 Location gp160 (376–384)
Author Location gp120 (376–384 IIIB)
Epitope FNCGGEFFY
Immunogen HIV-1 infection
Species (MHC) human (A29)
References Wilson *et al.* 1997a
- This is the optimal peptide for two CTL clones derived from two different donors.
- FNCRGEFFY and FNCRGGFFY are major and minor autologous variants in one of the donors, and showed reduced or no stimulatory activity for CTL from the host.
- The IIIB form and the form FNCAGEFFY were present in the other donor, and the CTL line had reduced activity with the FNCAGEFFY form relative to the index peptide.

HXB2 Location gp160 (376–384)
Author Location gp120 (376–384 IIIB)
Epitope PNCGGEFFY
Immunogen HIV-1 infection
Species (MHC) human (A29)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a
- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- PNCRGEFFY was an escape variant.

HXB2 Location gp160 (376–384)
Author Location gp120 (376–384 LAI)
Epitope FNCGGEFFY
Epitope name E2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A29)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location gp160 (376–384)
Author Location gp120
Epitope FNCGGEFFY
Immunogen HIV-1 infection
Species (MHC) human (A29)
Assay type Intracellular cytokine staining
Keywords immunodominance, genital and mucosal immunity
References Kaul *et al.* 2003

- Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher.
- The immunodominant response was to this epitope in the PBMC of 1/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).

HXB2 Location gp160 (376–384)
Author Location gp120 (376–384)
Epitope FNCGGEFFY
Epitope name FNC
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- One of the 7/8 study subjects that were HLA B8 recognized this CTL epitope.
- Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197.

HXB2 Location gp160 (376–384)
Author Location gp160
Epitope FNCGGEFFY
Epitope name FNC
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location gp160 (376–387)
Author Location gp120 (381–392 BRU)
Epitope KNCGGEFFYCNS
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dadaglio *et al.* 1991

- Defined through blocking CTL activity, and Env deletions.

HXB2 Location gp160 (377–386)
Author Location gp160 (374–383 SUMA)
Epitope NCGGEFFYCN
Epitope name gp160 NN10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.

- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location gp160 (377–387)
Author Location gp120 (377–387)
Epitope NSGGEFFYSNS
Immunogen
Species (MHC) human (A2)
References Hickling *et al.* 1990

- Peptides recognized by class I restricted CTL can bind to class II.

HXB2 Location gp160 (383–391)
Author Location gp120 (385–393)
Epitope FYCNTTQLF
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 1/4 HIV-1 + people tested.
- FYCNTTQLF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location gp160 (383–391)
Author Location gp160 (380–389 SUMA)
Epitope FYCNTTQLF
Epitope name GP160 FF9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.

- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location gp160 (410–429)
Author Location gp120 (410–429 PV22)
Epitope GSDTITLPCRIKQFINMWQE
Immunogen in vitro stimulation or selection
Species (MHC) human (DRA CD4+)
References Bouhdoud *et al.* 2000

- CTL were studied through PBMC stimulation *in vitro* by gp120 pulsed autologous monocytes.
- Human CD4+ CTL clone (Een217) is an MHC class II HLA-DRA restricted CTL clone that can lyse antigen presenting HLA-DRA-transfected murine L cells – natural variants of the epitope resulted in an anergic response.
- Low concentrations of the HXB2-derived variant (GSDTITLPCRIKQIINMWQK) induced T cell anergy – higher concentrations could induce proliferation and cytotoxic activity.
- CDC42 (TGDIITLPCRIKQII-NRWQV), Eli (TNTNITLQCRIKQIIKMVAG) and Z3 (CTGNITLPCRIKQIIMNWQE) variants did not induce proliferation, cytotoxic or anergic responses.

HXB2 Location gp160 (416–424)
Author Location Env (413–421 SF2)
Epitope LPCRIKQII
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords inter-clade comparisons, rate of progression
References Tomiyama *et al.* 1999

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed.
- Four of the six epitopes were highly conserved among B subtype sequences, LPCRIKQII is not conserved.

HXB2 Location gp160 (416–424)
Author Location gp160 (416–424 LAI)
Epitope LPCRIKQII
Subtype B
Immunogen
Species (MHC) human (B*5101)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5101 epitope.

HXB2 Location gp160 (416–424)
Author Location gp120 (378–385)
Epitope LPCRIKQII
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B51)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location gp160 (416–424)
Author Location gp160 (416–429)
Epitope LPCRIKQII
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these epitopes, but this increased over time.

HXB2 Location gp160 (416–429)
Author Location gp120 (410–429 H3DCG)
Epitope LPCRIKQFINMWQE
Immunogen HIV-1 infection
Species (MHC) human (DR4 CD4+)
References Siliciano *et al.* 1988

- CD4+ CTL restricted by class II HLA-DR4, targets primed by CD4 mediated uptake of gp120.

HXB2 Location gp160 (416–435)
Author Location gp120 (421–440 LAI)
Epitope LPCRIKQFINMWQEVGKAMY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dadaglio *et al.* 1991

- Defined through blocking CTL activity, and Env deletions.

HXB2 Location gp160 (419–427)
Author Location gp120 (424–432 HXB2)
Epitope RIKQIINMW
Subtype B
Immunogen
Species (MHC) human (A*3201)
References Harrer *et al.* 1996b

- C. Brander notes that this is an A*3201 epitope in the 1999 database.

HXB2 Location gp160 (419–427)
Author Location gp120 (419–427 HXB2)
Epitope RIKQIINMW
Subtype B
Immunogen
Species (MHC) human (A*3201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*3201 epitope.

HXB2 Location gp160 (419–427)
Author Location gp120 (419–427)
Epitope RIKQIINMW?
Immunogen HIV-1 infection
Species (MHC) human (A29, A32)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was A29 and responded to RIKQIINMW, and another responder was A32 and these are thought to be presenting molecules.
- The sequence is unclear – Betts calls both peptide 30 and peptide 32 gp120 419–427 and the peptide sequences are not provided.

HXB2 Location gp160 (419–427)
Author Location gp120 (424–432 LAI)
Epitope RIKQFINMW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A32)
References Ray *et al.* 1998

- Autologous virus was used to detect CTL in two individuals, and in both cases strain-specific autologous CTL were found.
- The autologous epitope sequence was RIKQIINMW, MN and RF were KIKQFINMW and RIKQFVNMW respectively, and all were reactive with CTL clones.

HXB2 Location gp160 (419–427)
Author Location gp120 (420–428)
Epitope RIKQIINMW
Immunogen HIV-1 infection
Species (MHC) human (A32)
References Ferris *et al.* 1999

- This epitope is processed by a TAP1/2 dependent mechanism.

HXB2 Location gp160 (419–427)
Author Location gp120
Epitope RIKQIINMW

Epitope name A32-RW10(gp120)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A32)
Donor MHC A32, A?, B44, B?; A30, A32, B18, B27
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient B displayed the greatest response to epitope B44-AW11(p24) and also responded to A32-PW10(RT) in both PB and LN samples, while a third response against epitope A32-RW10(gp120) was only detected in the LN sample. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).

HXB2 Location gp160 (421–435)
Author Location gp120 (421–440 LAI)
Epitope KQFINMWQEVGKAMY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dadaglio *et al.* 1991

- Defined through blocking CTL activity, and Env deletions.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Immunogen HIV-1 exposed seronegative
Species (MHC) human
References Pinto *et al.* 1995

- CTL and T helper cell reactivity in healthcare workers exposed to HIV.

HXB2 Location gp160 (421–436)
Author Location gp120 (MN)
Epitope KQIINMWQEVGKAMYA
Immunogen HIV-1 infection
Species (MHC) chimpanzee
References Lubeck *et al.* 1997

- Epitope-specific CTL detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant.
- CTL response may account for protection against subsequent HIV-1 SF2 challenge in a chimpanzee lacking neutralizing antibodies.
- Helper and cytotoxic T cells can be stimulated by this peptide (T1)

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Clerici *et al.* 1991a

- Helper and cytotoxic T cells can be stimulated by this peptide (T1)

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Cease *et al.* 1987

- Helper and cytotoxic T cells can be stimulated by this peptide (T1)

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) mouse (H-2$^{a, b, f}$)
References Shirai *et al.* 1992

- In a murine system multiple class I molecules can present to CTL.

HXB2 Location gp160 (425–434)
Author Location Env
Epitope NMWQEVGKAM
Epitope name 1257
Subtype multiple
Immunogen HIV-1 infection
Species (MHC) human (A2)
Donor MHC A02, A30, B39,?, ?; A02, A03, B44,?, Cw05, Cw07
Country United States.
Assay type T-cell Elispot
Keywords binding affinity, computational epitope prediction
References De Groot *et al.* 2003

- Epitopes defined using sequence parsing and matching algorithm Conservatrix, and epitope prediction tool EpiMatrix, were shown to be conserved in a broad range of HIV-1 sequences derived from different parts of the world. 31 novel highly conserved HIV-1 epitopes were found, among which four were recognized as promiscuous epitopes and five as MHC supertypes.
- Estimated binding probability for NMWQEVGKAM: 50%

HXB2 Location gp160 (432–451)
Author Location gp120 (439–458 IIIB)
Epitope KAMYAPPISGQIRCSSNITG
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* CD4BS, Gag, gp120, V3
Species (MHC) macaque
References Wagner *et al.* 1998b

- A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock.
- CTL specific for this epitope could be found both before and after SHIV challenge.

HXB2 Location gp160 (434–443)
Author Location gp120 (431–440)
Epitope MYAPPIGGQI
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-2K^{d})
References Duarte *et al.* 1996

- Tolerization of CTL response with continued administration of soluble peptide.

HXB2 Location gp160 (435–443)
Author Location Env (89.6)
Epitope YAPPISGQI
Epitope name p41A
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade 89.6, SIV *HIV component:* Env, Gag *Adjuvant:* IL-2/Ig
Species (MHC) macaque
References Barouch *et al.* 2000; Shen & Siliciano 2000

- Different HIV strains were used for different regions: SIVmac239 Gag and HIV-1 89.6P Env
- Monkeys that received the DNA vaccines augmented with IL-2/Ig were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, stable CD4+ T-cell counts, preserved virus-specific CD4+ T-cell responses, low to undetectable viral loads, and no evidence of disease or mortality by day 140 after challenge – monkeys that got a sham vaccine had high viral load, progressed to disease, and were half were dead by day 140.
- IL2/Ig consisting of interleukin-2 (IL-2) for immune stimulation, and the Fc portion of immunoglobulin G (IgG) for stability, was delivered either as protein or as DNA – both enhance the CTL response to vaccination, DNA IL2/Ig giving the most intense response.
- Responses to a dominant Mamu A*01 gag epitope SIV Gag p11C (CTPYDINQM) and a subdominant epitope HIV-1 Env p41A (YAPPISGQI) were tracked and had good durability prior to challenge, and the higher the prechallenge peak p11C CTL response, the lower the post-challenge viral load.
- No NAb responses were detected in the vaccinated monkeys prior to challenge, and comparable peak NAb titers developed in vaccinated monkeys and control monkeys with preserved CD4+ T-cells.
- Shen *et al.* 2000 is an accompanying commentary.

HXB2 Location gp160 (435–443)
Author Location Env (89.6)
Epitope YAPPISGQI
Epitope name p41A
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade 89.6, SIV *HIV component:* Env, Gag-Pol *Adjuvant:* IL-2/Ig
Species (MHC) macaque
Keywords immunodominance
References Barouch *et al.* 2001b

- Different HIV strains were used for different regions: SIVmac239 Gag/Pol and HIV-1 89.6P Env
- Four monkeys were vaccinated with a modified vaccinia Ankara (MVA) vaccine that elicited strong CTL to the immunodominant SIV gag epitope in 4/4 animals, and 1/4 made a response to the HIV Env epitope YAPPISGQI, as determined by tetramer staining and chromium release assays.
- The animals were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, secondary NAb responses upon challenge, partial preservation of CD4+ T-cell counts, lower viral loads, and no evidence of disease or mortality by day 168 after challenge – monkeys that got a sham vaccine had high viral load, progressed to disease, and 2/4 were dead by day 168.

HXB2 Location gp160 (435–443)
Author Location
Epitope YAPPISGQI
Immunogen SHIV infection
Species (MHC) macaque (Mamu-A*01)
References Egan *et al.* 1999

- SHIV-infected rhesus macaques have high frequencies of response to the SIVmac epitope gag p11C,C-M (CTPYDINQM) but only a fraction of A*01 monkeys tested have responses to SIVmac pol epitope STPPLVRLV and HIV-1 env epitope YAPPISGQI.

HXB2 Location gp160 (435–443)
Author Location gp41 (89.6)
Epitope YAPPISGQI
Epitope name p41A
Immunogen SHIV infection, Vaccine
Vector/Type: DNA, modified vaccinia Ankara (MVA) *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Env, Gag *Adjuvant:* IL-2/Ig
Species (MHC) macaque (Mamu-A*01)
Keywords immunodominance
References Barouch *et al.* 2001a

- Mamu-A*01+ rhesus monkeys infected with SHIV-89.6 and SHIV-HXBc2 make immunodominant responses to SIV Gag p11C epitope (CTPYDINQM) and a subdominant response to HIV-1 Env p41A epitope (YAPPISGQI)

- The binding affinities are the same for the two Mamu A*01 epitopes, so that is not what dictates the dominance.
- Monkeys vaccinated with MVA vectors carrying SIV gag/pol and HIV-1 env showed the same p11C epitope dominance and p41A epitope subdominance, but co-dominance was observed and the response to p41A increased when DNA vaccination was done using the SIV and HIV genes under CMV promotor control with IL2-IG adjuvant.

HXB2 Location gp160 (435–443)
Author Location Env
Epitope YAPPISGQI
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade 89.6P, SIV *HIV component:* Env, Gag
Species (MHC) macaque (Mamu-A*01)
Assay type Flow cytometric CTL assay
Keywords vaccine-specific epitope characteristics, rate of progression, kinetics, memory cells, characterizing CD8+ T cell responses
References Davenport *et al.* 2004

- Activation and expansion of antigen-specific CD8+ T-cells shows a delay following infection that allows early viral replication. Until day 10, the kinetics of CD8+ T-cell expansion was the same in vaccinated and control macaques. An increase in virus-specific CD8+ T-cell numbers around day 10 in vaccinated macaques coincides with a slowing in viral replication. This indicates that while cytotoxic T-lyphocyte-inducing vaccines may have a long-term benefit in controling viral replication and preventing disease progression, they cannot prevent infection.

HXB2 Location gp160 (444–453)
Author Location Env
Epitope RCSSNITGLL
Immunogen
Species (MHC) human (B56)
References De Groot *et al.* 2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 of the predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay.
- RCSSNITGLL was newly defined as an epitope in this study, and was shown to stimulate an ELISPOT response, despite not detectably binding to HLA-B7.

HXB2 Location gp160 (486–494)
Author Location gp160 (485–493 SUMA)
Epitope YKVVKIEPL
Epitope name GP160 YL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, acute infection, characterizing CD8+ T cell responses
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Only four epitopes were found to acquire escape muations in SUMA over time, and this was one of the 20 that remained invariant. A low level response was detected at acute infection that persisted through early infection.

HXB2 Location gp160 (489–508)
Author Location Env (496–506 BH10, LAI)
Epitope VKIEPLGVAPTKAKRRVVQR
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is VAPTKAKRRVV) has similarity with the mast/stem cell growth factor receptor precursor fragment VVPTKADKRRSV.

HXB2 Location gp160 (489–508)
Author Location Env (497–512 BH10, LAI)
Epitope VKIEPLGVAPTKAKRRVVQR
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is APTKAKRRVVQREKRA) has similarity with the human interferon-related IFRD2 (PC4-B) protein fragment ARTKARSRVRDKRA.

HXB2 Location gp160 (489–508)
Author Location gp120 (494–513 BRU)
Epitope VKIEPLGVAPTKAKRRVVQR
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Dadaglio *et al.* 1991

- Defined through blocking CTL activity, and Env deletions.

HXB2 Location gp160 (519–543)

Author Location gp41 (519–543)
Epitope FLGFLGAAGSTMGAASLTLTVQARC
Immunogen HIV-1 infection
Species (MHC) human (Cw7)
References Nehete *et al.* 1998a

- Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one.
- HLA-C antigens are expressed on lymphoid cells to a lesser extent, 10% of either HLA-A or HLA-B.
- HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing.

HXB2 Location gp160 (529–537)
Author Location Env (529–)
Epitope TMGAASITL
Epitope name Env529
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* gp160 *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was an intermediate A2 binder that did not induce CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 5/17 HIV+ HLA-A2 subjects.

HXB2 Location gp160 (552–571)
Author Location Env (552–571)
Epitope QSNLLRAIEAQQHMLQLTVW
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location gp160 (557–565)
Author Location gp41 (557–565 IIIB)
Epitope RAIEAQQHL
Immunogen HIV-1 infection
Species (MHC) human
Keywords responses in children, mother-to-infant transmission
References Wilson *et al.* 1996

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.
- RAIDAQQHL and RVIEAQQHL, naturally occurring variants, were found in mother and are recognized.

HXB2 Location gp160 (557–565)
Author Location gp41 (557–565)
Epitope RAIEAQQHL
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was HLA A*0201, A32, B60, B78, and responded to RAIEAQQHL, previously noted to be B51.

HXB2 Location gp160 (557–565)
Author Location gp41 (557–565 IIIB)
Epitope RAIEAQQHL
Immunogen HIV-1 infection
Species (MHC) human
Keywords mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- This epitope was invariant in both the mother and her infant.

HXB2 Location gp160 (557–565)
Author Location Env (555–567 BH10, LAI)
Epitope RAIEAQQHL
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is LLRAIEAQQHLL) has similarity with human MHC class II regulatory factor RFX1 fragment LLRLMEDQQHMA.

HXB2 Location gp160 (557–565)
Author Location gp41 (557–665)
Epitope RAIEAQQWQ
Epitope name E3
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords HAART, ART, escape

References Samri *et al.* 2000
- The epitope was recognized by patient 246#1 in a study of the effects of therapy escape mutations on CTL recognition.

HXB2 Location gp160 (557–565)
Author Location gp160 (557–565)
Epitope RAIEAQQHL
Immunogen HIV-1 infection
Species (MHC) human (B15, 51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003
- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location gp160 (557–565)
Author Location gp41 (557–565 IIIB)
Epitope RAIEAQQHL
Immunogen HIV-1 infection
Species (MHC) human (B51)
References Sipsas *et al.* 1997
- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.
- KAIEAQQHL, a variant found in HIV-1 NY5CG, was also recognized.
- RAIEAQQHM, a variant found in HIV-1 JRCSF, was also recognized.
- RAIDAQQHL, a variant found in HIV-1 ETR, was also recognized.
- RAIKAQQHL, a variant found in HIV-1 CDC42, was also recognized.

HXB2 Location gp160 (557–565)
Author Location gp41 (557–565)
Epitope RAIEAQQHL
Immunogen HIV-1 infection
Species (MHC) human (B51)
References Ferris *et al.* 1999
- This epitope can be processed by a TAP1/2 dependent mechanism.

HXB2 Location gp160 (557–565)
Author Location gp41 (557–565)
Epitope RAIEAQQWQ
Epitope name RAI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000
- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- None of the 8 study subjects recognized this epitope but none were HLA B51+

HXB2 Location gp160 (557–565)
Author Location gp41 (47–55)
Epitope RAIEAQQHL
Immunogen HIV-1 infection
Species (MHC) human (B51)
References Ferrari *et al.* 2000
- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location gp160 (557–565)
Author Location gp41 (557–565 LAI)
Epitope RAIEAQQHL
Epitope name E3
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B51)
Keywords HAART, ART
References Mollet *et al.* 2000
- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location gp160 (557–565)
Author Location Env (gp160) (557–565)
Epitope RAIEAQQHL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw*0304)
Keywords inter-clade comparisons
References Currier *et al.* 2002a
- Cross-reactive responses were found in PBMC isolated from individuals infected with either B or CRF01_AE clade viruses, as determined by Elispot assays of target cells expressing recombinant vaccinia viruses expressing HIV-1 gag, env, nef and pol from many clades.

- CTL from subject US101, infected with a clade B virus, displayed broad cross-reactivity to HIV-1 clade A, B, C, D, CRF01_AE, F G, recognized this epitope. Clade B and C had a L->M change in the C-term position that was tolerated. The H clade Env was not cross-reactive, and had the sequence RAIAARQHM.

HXB2 Location gp160 (557–565)
Author Location gp41 (46–54)
Epitope RAIEAQQHL
Immunogen
Species (MHC) human (Cw*0304)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (557–565)
Author Location (C consensus)
Epitope RAIEAQQHM
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (Cw*0801)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location gp160 (557–565)
Author Location gp41 (46–54)
Epitope RAIEAQQHL
Immunogen
Species (MHC) human (Cw*15)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (565–573)
Author Location Env (565–)
Epitope LLQLTVWGI
Epitope name Env565
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Env *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced CD8+ T-cell IFN gamma responses in mice. Responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.

HXB2 Location gp160 (565–573)
Author Location Env (731–739)
Epitope LLQLTVWGI
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).

HXB2 Location gp160 (570–589)
Author Location gp41 (571–590 LAI)
Epitope VWGIKQLQARILAVERYLKD
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia prime with gp160 boost *Strain:* B clade LAI *HIV component:* gp160
Species (MHC) human (DR-1 CD4+ CTL)
References Kent *et al.* 1997a

- VWGIKQLQARILAVERYLKD, present in HIV-1 LAI, was the immunizing strain.
- VWGIKQLQARVLAVERYLKD, present in HIV-1 MN, was also recognized.
- VWGIKQPQARVLAVERYLRD was the form carried by the autologous strain that infected the vaccinee.
- Lysis of the target cells by CD4+ CTL was inhibited with the addition of the peptide representing the autologous strain.
- The infecting virus epitope also antagonized the proliferative functions of the CD4+ CTL clone.
- The behavior of the autologous strain presents a possible mechanism for vaccine failure since the infecting virus not only escapes CTL activity, but inhibits the ability of CTL to recognize other variants.

HXB2 Location gp160 (572–590)
Author Location gp41 (572–590 BRU)
Epitope GIKQLQARILAVERYLKDQ
Immunogen Vaccine

Vector/Type: protein *Strain:* B clade BRU
HIV component: gp160
Species (MHC) human (DPw4.2)
References Hammond *et al.* 1991
- CD4+ CTL.

HXB2 Location gp160 (575–599)
Author Location gp41 (575–599 IIIB)
Epitope QLQARILAVERYLKDQQLLGIWGCS
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Jassoy *et al.* 1992
- Epitope recognized by CTL clone derived from CSF.

HXB2 Location gp160 (583–592)
Author Location gp41 (583–592 PV22)
Epitope VERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Jassoy *et al.* 1993
- HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human
References Price *et al.* 1995
- Study of cytokines released by HIV-1 specific activated CTL.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human
References Borrow *et al.* 1994
- Three out of five patients with HIV-1 symptomatic infection controlled their viral infection well and mounted an early, strong HIV-1 specific MHC restricted CTL response.
- One of the three, study subject BORI, specifically recognized this peptide.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592 HXB2)
Epitope ERYLKDQQL
Epitope name E4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A32, B14)
Keywords HAART, ART
References Mollet *et al.* 2000
- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location gp160 (584–592)
Author Location gp41
Epitope ERYLRDQQL
Immunogen HIV-1 infection
Species (MHC) human (B*14)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002
- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.
- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location gp160 (584–592)
Author Location (C consensus)
Epitope ERYLKDQQL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*14)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004
- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592 PV22)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B*1402)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*1402 epitope.

HXB2 Location gp160 (584–592)
Author Location gp160 (598–597 BORI, SUMA)
Epitope ERYLKDQQL
Epitope name gp160 EL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1402)
Donor MHC A*2902, B*1402, C*0802; A*1103, A*2402, B*1402, B*1501, C*0802
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, escape, acute infection, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient BORI had high viral loads and rapid CD4 decline. BORI mounted 8 detected responses. BORI did not control viral replication well, and escape mutations occurred early and in most epitopes, 6/7 that were precisely identified.
- The patient SUMA maintained low viral loads and stable CD4 T cell counts through seven years of follow up. In contrast to more rapid progressors, WEAU and BORI, SUMA a broad response to 24 epitopes, with little immunodominance. Two peptides were somewhat more intensely recognized in acute infection, but this response leveled out early on.
- Eleven variants in the ERYLKDQQL epitope were found in the patient BORI. ERYLKeQQp came up first at day 17 from onset of symptoms, but wasn't tested for escape properties. ERYLrDQQL came up next, by day 31, but didn't confer escape in a Cr release assay. By day 218, three variants were found, all of which gave a diminished response: ERYLtDQQL, ERYLqDQQL, and ERYLsDQQL. By day 556 a complex mixture was present, also including the ERYLmDQQL variant that gave a further reduction in the response, and many double mutants: ERYLmDQrL, ERYLmDrQL, ERYLmDQlL, ERYLtDQrL and ERYrtDQrL.
- In SUMA, the only variation found in the 24 epitopes was in three overlapping epitopes in Tat, and in this gp160 epitope; variation accumulated early in infection in the Tat epitopes, but this epitope was stable until a sample 736 days post-infection, when only the ERYLqDQQL variant was detected. This variant was not tested with CTL from SUMA, but gave a diminished response in BORI.

HXB2 Location gp160 (584–592)
Author Location gp41
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Wagner *et al.* 1998a

- CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords HAART, ART
References Kalams *et al.* 1999b

- Two patients were followed before and after HAART – reduced plasma HIV-1 RNA levels resulted in a decline in HIV *in vivo* activated specific CTL such that by day 260 CTL activities were undetectable.
- ERYLKDQQL was the dominant response in one of the individuals, SLYNTVATL subdominant.
- Sporadic breakthrough in viremia resulted in increases in CTLp.
- Peptide-tetramer staining demonstrated that declining levels of *in vivo*-activated CTL were associated with a decrease in expression of CD38.
- Memory CTL frequency directed against Vac-Gag, Vac-RT, Vac-Env, and Vac-Nef initially increased with HAART and then decreased with the decline of the viral load.

HXB2 Location gp160 (584–592)
Author Location gp41 (591–599 SF2)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-A3, -A32, -B7, -B14.

HXB2 Location gp160 (584–592)
Author Location gp41 (591–599 SF2)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords inter-clade comparisons
References Cao *et al.* 1997a

- The consensus sequence for clades B, C, and D is ERYLKDQQL.
- The consensus sequence for clade A is ERYLRDQQL and it is equally reactive.
- The consensus sequence for clade E is ERYLKDQKF and it is not reactive.

HXB2 Location gp160 (584–592)
Author Location gp41
Epitope ERYLKDQQL
Immunogen HIV-1 exposed seronegative

Species (MHC) human (B14)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A and D subtype consensus are identical to the B clade epitope, ERyLkDQQL.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Sipsas *et al.* 1997

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Yang *et al.* 1996

- CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL.
- Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones.
- The distinction was thought to be due to lower expression of RT relative to Env and Gag.
- CTL can lyse infected cells early after infection, possibly prior to viral production.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
Assay type CTL suppression of replication
References Yang *et al.* 1997a

- CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*.
- CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation.
- CTL suppress HIV replication more efficiently in HLA-matched cells.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592 PV22)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Johnson *et al.* 1992

- Two overlapping CTL epitopes were mapped with different HLA restriction (also see YLKDQQLL HLA-B8)

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592 PV22)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Jassoy *et al.* 1993

- HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592 HXB2)
Epitope ERYLKDQQL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Kalams *et al.* 1994; Kalams *et al.* 1996

- Longitudinal study of T cell receptor usage in a single individual.
- Persistence of oligoclonal response to this epitope for over 5 years.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen Peptide-HLA interaction
Species (MHC) human (B14)
References DiBrino *et al.* 1994a

- Epitope studied in the context of HLA-B14 binding.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Hammond *et al.* 1995

- This peptide can be processed for HLA-B14 presentation in a TAP-1/2 independent pathway.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Kalams *et al.* 1996

- CTL response to this epitope was studied in 5 HLA-B14 positive persons.
- CTL responses were detected in all five, and CTL clones were isolated from 4/5.
- A diverse repertoire of TCRs recognized this epitope, with similar fine specificities.
- 3/5 subjects showed no variation in viral sequence, 2/5 had a dominant variant that resulted in poor recognition, ERYLQDQQL.
- A minor CTL response specific for the ERYLQDQQL could be detected by two individuals, but the major CTL response was to the ERYLKDQQL form even when it was the minority form.
- Some single amino acid substitutions were well tolerated by most of the CTL clones tested, but others, particularly in the center three amino acid positions, abrogated peptide stimulatory activity.

HXB2 Location gp160 (584–592)
Author Location gp120 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Ferris *et al.* 1999; Hammond *et al.* 1995

- This epitope is processed by both TAP1/2 dependent and independent mechanisms.

HXB2 Location gp160 (584–592)
Author Location gp41
Epitope ERYLKDQQL
Immunogen
Species (MHC) human (B14)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective.
- HIV-2 sequence: EKYLQDQAR – no cross-reactivity Johnson *et al.* [1992]

HXB2 Location gp160 (584–592)
Author Location gp41 (SF2)
Epitope ERYLKDQQL
Epitope name EL9
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords acute infection
References Goulder *et al.* 2001a

- Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia.
- A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation.
- Recognized by two A*0201-positive chronically infected subjects.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Epitope name 588K
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords HAART, ART, TCR usage
References Islam *et al.* 2001

- Transcript frequencies of four CTL clones from patient 115, with a chronic and stable HIV-1 infection, were tracked in a longitudinal study of samples collected 6-11 years post infection: clone M21 and E15 recognize ERYLKDQQL,and clone D87 recognizes variant ERYLQDQQL, and clone p175b recognizes the A2 epitope SLYNTVATL.
- CTL clone M21 uses the Vβ 4, CDR3 VKDGA, Jβ 1.2 TCR beta gene, and clone E15 uses the Vβ 4, CDR3 VEDWGGAS Jβ 2.1 TCR beta gene, and D87 uses Vβ8, ALNRVD, Jβ2.1.
- Responses were stable even through HAART with undetectable viral loads but frequencies varied over time by 100-fold, ranging from 0.012% of the total population for SLYNTVATL at its lowest point to 3.78% for M21, with the relative frequencies of clones shifting over time.

HXB2 Location gp160 (584–592)
Author Location gp41 (589–597 SF2)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B14+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/2 group 2, and 0/0 group 3.

HXB2 Location gp160 (584–592)
Author Location gp41 (589–597)
Epitope ERYLRDQQL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B14)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location gp160 (584–592)
Author Location gp41 (JRCSF)
Epitope ERYLKDQQL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Severino *et al.* 2000

- Primary HLA-B14+ CD4+ CD3+ and HLA-mismatched lymphocytes from uninfected donors were infected with JRCSF after isolation then cocultured with the B14-restricted CTL clone 15160/D75 specific for ERYLKDQQL, and viral inhibition was MHC-restricted.
- Primary monocytes and monocyte-derived DC were generated from the same donors, replication of HIV-1 in these cell types was less efficient than in lymphocytes and could also be inhibited by MHC-restricted CTL.

- DC-lymphocyte cluster cultures allowed vigorous viral replication and MHC-restricted CTL viral inhibition was blunted or lost depending on the ratio of DC to CD4+ lymphocyte in the culture.

HXB2 Location gp160 (584–592)
Author Location gp41 (SF2)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.

HXB2 Location gp160 (584–592)
Author Location Env (589–597)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords early-expressed proteins, kinetics
References Guillon *et al.* 2002b

- An early-expressed Nef protein was modified to contain Env and Pol epitopes to enable the study the effect of expression kinetics on CTL mediated suppression of replication. The "EpiNef" construct was inserted into a recombinant vaccinia virus which was used to infect a target cell line; the target cells were lysed by CTL clones specific for the Env and Pol epitopes indicating that they were properly processed.

HXB2 Location gp160 (584–592)
Author Location gp41 (584–592)
Epitope ERYLKDQQL
Immunogen HIV-1 infection
Species (MHC) human (B14)
Keywords class I down-regulation by Nef
References Yang *et al.* 2002

- Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed *in vitro* than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL43 infected cells. The CTL clone 15160D75, specific for the class I B14 presented epitope ERYLKDQQL, was one of four used in this study.

HXB2 Location gp160 (584–592)
Author Location gp41
Epitope ERYLKDQQL
Epitope name B14-EL9(gp41)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Donor MHC A32, A?, B7, B14
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT).

HXB2 Location gp160 (584–592)
Author Location gp41
Epitope ERYLKDQQL
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade
HIV component: p17 Gag, p24 Gag
Species (MHC) human (B14)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location gp160 (584–592)
Author Location gp41 (73–81)

Epitope ERYLKDQQL
Epitope name Env EL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Assay type Chromium-release assay
Keywords binding affinity, TCR usage, characterizing CD8+ T cell responses
References Yang *et al.* 2003b

- Killing efficiency of CTLs and their ability to suppress viral replication is shown to depend more on epitope specificity than to antigenic avidity. Different clones recognizing the same epitope had similar killing efficiency despite their variation in avidity. Nef specific CTL clones tended to be most inhibitory, followed by Gag, then by RT specific clones, regardless of avidity.
- 4/14 CTL T-cell clones tested were specific for Env EL9. Under conditions of excess peptide (100ug/ml), there was no difference in their lytic potential; all possessed similar effector capacity. Avidity was measured as the sensitizing dose of peptide required for 50% of maximal killing (SD50), which varied from 20 pg/ml to 100 ng/ml, over four orders of magnitude for all 14 epitopes. The SD50 range for Env EL9 was 5,000 - 60,000 pg/ml.

HXB2 Location gp160 (584–592)
Author Location (B consensus)
Epitope ERYLKDQQL
Epitope name EL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B14)
Donor MHC A28, A29, B14, B44, Cw8; A25, A32, B08, B14, Cw7, Cw8
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 2/9 individuals recognized this epitope, presented by HLA-B14.

HXB2 Location gp160 (584–592)
Author Location gp41 (subtype B)
Epitope ERYLKDQQL
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B14, B*1402)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among B and D clade viruses.
- The Clade A version of the epitope is ERYLRDQQL.

HXB2 Location gp160 (584–594)
Author Location gp41 (584–594)
Epitope ERYLKDQQLLG
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A1, A1, B8, B14, Cw7, Cw8
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location gp160 (585–592)
Author Location gp41 (584–591 SF2)
Epitope RYLRDQQL
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 2/4 HIV-1 + people tested.
- RYLRDQQL bound to A*2402 weakly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location gp160 (585–592)
Author Location gp41 (590–597 LAI)
Epitope RYLKDQQL

Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Shankar *et al.* 1996

HXB2 Location gp160 (585–593)
Author Location gp41 (74–82)
Epitope RYLKDQQLL
Immunogen HIV-1 infection
Species (MHC) human (A*23)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (585–593)
Author Location gp41 (585–593)
Epitope RYLKDQQLL
Immunogen HIV-1 infection
Species (MHC) human (A*2301)
Donor MHC A*2301, B*3501, B*1503 (B72), Cw2, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location gp160 (585–593)
Author Location gp41 (584–591 SF2)
Epitope RYLRDQQLL
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 4/4 HIV-1 + people tested.
- RYLRDQQLL bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location gp160 (585–593)
Author Location gp41 (591–598 LAI)
Epitope RYLKDQQLL
Subtype B
Immunogen
Species (MHC) human (A*2402)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*2402 epitope.

HXB2 Location gp160 (585–593)
Author Location (C consensus)
Epitope RYLKDQQLL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location gp160 (585–593)
Author Location gp41
Epitope RYLKDQQLL
Epitope name A24-RL9(gp41)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A24)
Donor MHC A24, A?, B7, B27
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.

- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).

HXB2 Location gp160 (585–593)
Author Location Env
Epitope RYLKDQQLL
Epitope name RW8
Immunogen HIV-1 infection
Species (MHC) human (A24)
Donor MHC A2, A24, B38, B60, Cw2, Cw12
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early treatment
References Montefiori *et al.* 2003

- HIV-1 + patient AC10 underwent early HAART treatment, which was discontinued 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.

HXB2 Location gp160 (585–595)
Author Location gp41 (584–591 SF2)
Epitope RYLRDQQLLGI
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 4/4 HIV-1 + people tested.
- RYLRDQQLLGI bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location gp160 (585–595)
Author Location Env (584–594)
Epitope RYLRDQQLLGI
Epitope name Env584-11
Immunogen Vaccine
Vector/Type: Sendai virus vector system (SeV)
Species (MHC) human (A*2402)
References Kawana-Tachikawa *et al.* 2002

- A Sendai virus vector system (SeV) was developd that expressed HLA-A*2402-restricted class I/peptide complexes; this system could be used to detect responses and has the potential to elicit immune responses.
- MHC class I/peptide tetramers could be made using this system that bound to epitope-specific CTLs in PBMCs.
- Cells transfection with SeV modified to express A*2402-HIV epitope complexes induced CTL mediated specific cell lysis.

HXB2 Location gp160 (586–593)
Author Location gp160
Epitope YLRDQQLL
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls, ML887.

HXB2 Location gp160 (586–593)
Author Location gp41 (584–591 NL43)
Epitope YLKDQQLL
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Dai *et al.* 1992

- The lysine (K) is critical for eliciting a HLA-A24 CTL response.
- C. Brander notes that this is an A*2402 epitope in the 1999 database, and suggested that the epitope is RYLKQQLL.

HXB2 Location gp160 (586–593)
Author Location gp41 (591–598)
Epitope YLRDQQLL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A24)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- Variants (R)YL(R/K)DQQLL are specific for the A/B clade.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.

- Among HLA-A24 women, 3/4 HEPS and 10/10 HIV-1 infected women recognized this epitope, and (R)YL(R/K)DQQLL tended to be reactive in HEPS and infected women, RDYVDRFFKTL in infected women only.
- The dominant response to this HLA allele was to this epitope in all 3/4 HEPS cases but in only 4 of the 10/10 HIV-1 infected women.
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.

HXB2 Location gp160 (586–593)
Author Location gp41 (580–587 CM243 subtype CRF01)
Epitope YLKDQQLL
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A24)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- The only HLA-A24 FSW tested did not recognized the E clade version of this epitope RYLKDQKLL, which differs from the previously defined B clade version by one amino acid, YLKDQQLL, with an additional amino acid added on.

HXB2 Location gp160 (586–593)
Author Location gp41 (591–598)
Epitope YLKDQQLL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A24)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- One of seven patients responded to this peptide with GzB producing cells, and a different patient responded with IFN-gamma producing cells.

HXB2 Location gp160 (586–593)
Author Location gp41 (586–593 LAI)
Epitope YLKDQQLL
Epitope name E1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A24, B8)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location gp160 (586–593)
Author Location gp41 (subtype A)
Epitope YLKDQQLL
Subtype A
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade
HIV component: p17 Gag, p24 Gag
Species (MHC) human, macaque (A24, B8)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location gp160 (586–593)
Author Location gp41 (586–593)
Epitope YLKDQQLL
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0801 epitope.

HXB2 Location gp160 (586–593)
Author Location gp41 (586–593)
Epitope YLKDQQLL
Immunogen HIV-1 infection

Species (MHC) human (B8)
References Johnson *et al.* 1992
- Two overlapping CTL epitopes were mapped with different HLA restriction (also see ERYLKDQQL HLA-B14)

HXB2 Location gp160 (586–593)
Author Location gp41 (586–593)
Epitope YLKDQQLL
Immunogen Peptide-HLA interaction
Species (MHC) human (B8)
References Sutton *et al.* 1993
- Predicted epitope based on B8-binding motifs, from larger peptide QLQARILAVERYLKDQQLLGIWGCS.

HXB2 Location gp160 (586–593)
Author Location gp41 (76–83)
Epitope YLKDQQLL
Immunogen
Species (MHC) human (B8)
References Goulder *et al.* 1997g
- Included in a study of the B8 binding motif.

HXB2 Location gp160 (586–593)
Author Location gp41
Epitope YLKDQQLL
Immunogen
Species (MHC) human (B8)
References Rowland-Jones *et al.* 1999
- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive.
- HIV-2 sequence: YLQDQARL – no cross-reactivity Johnson *et al.* [1992]

HXB2 Location gp160 (586–593)
Author Location gp41 (586–593)
Epitope YLKDQQLL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B8)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location gp160 (586–593)
Author Location gp41 (586–593)
Epitope YLKDQQLL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Day *et al.* 2001
- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.

HXB2 Location gp160 (586–598)
Author Location gp41 (586–598)
Epitope YLRDQQLLGIWGC
Immunogen HIV-1 infection
Species (MHC) human (Cw7)
References Nehete *et al.* 1998a
- Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one.
- HLA-C antigens are expressed on lymphoid cells to a lesser extent, 10% of either HLA-A or HLA-B.
- HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing.

HXB2 Location gp160 (594–608)
Author Location gp41 (SF2)
Epitope GIWGCSGKLICTTAV
Epitope name Peptide2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B17(57))
Assay type Chromium-release assay
References Carmichael *et al.* 1996
- Cross-reactivity of Env-specific CTL clones from 14 seropositive HIV-1 infected patients was tested using peptides based on 3 B clade variants (MN, IIIB, and RF). The proportion of CTL clones that cross-recognized conserved variants was low. Most CTL clones recognized only one peptide variant, indicating most Env responses are not cross-reactive within the B clade.
- This HLA B17(57) epitope was newly identified within gp41 of HIV-1 SF2. SF2 and IIIB have identical sequences within this peptide, but the T-cell clone that recognizes this peptide does not recognize the MN (gFwgcsgklicttTv) or RF (giwgcsgklicttTv) variants of this peptide.

HXB2 Location gp160 (594–608)
Author Location gp41
Epitope GIWGCSGKLICTTAV
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Jin *et al.* 1998b
- Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction.
- Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK.

HXB2 Location gp160 (606–614)
Author Location gp41 (605–615 LAI)
Epitope TAVPWNASW
Subtype B
Immunogen Vaccine

Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*3501 epitope.

HXB2 Location gp160 (606–614)
Author Location gp41 (606–614 HXB2)
Epitope TAVPWNASW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords epitope processing
References Ferris *et al.* 1996
- Natural form of this peptide is not glycosylated, suggesting initial Class I processing may occur in the cytosol.

HXB2 Location gp160 (606–614)
Author Location gp41 (605–615 LAI)
Epitope TAVPWNASW
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (B35)
References Johnson *et al.* 1994b
- Epitope for vaccine induced CD8+ clone.

HXB2 Location gp160 (606–614)
Author Location gp41 (606–614 LAI)
Epitope TAVPWNASW
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (B35)
References Johnson *et al.* 1994a
- HLA restricted CTL response to epitope in HIV-1 vaccinia-env vaccinees.

HXB2 Location gp160 (606–614)
Author Location gp41 (606–614 LAI)
Epitope TAVPWNASW
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) human (B35)
References Hammond *et al.* 1995
- Peptide only processed by a TAP-1/2-dependent pathway.

HXB2 Location gp160 (606–614)
Author Location gp41 (606–614)
Epitope TAVPWNASW
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Ferris *et al.* 1999
- This epitope is processed by a TAP1/2 dependent mechanism.

HXB2 Location gp160 (606–614)
Author Location gp41 (subtype B)
Epitope TAVPWNASW
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B35)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b
- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among A, B and D clade viruses.

HXB2 Location gp160 (606–614)
Author Location gp41 (606–614)
Epitope TAVPWNASW
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B35)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location gp160 (606–614)
Author Location gp41 (606–614)
Epitope TAVPWNASW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Donor MHC A3, A33, B14, B35, Cw*0401, Cw0802
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003
- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.

- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location gp160 (606–614)
Author Location Env (96–104)
Epitope TAVPWNASW
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/9 patients recognized this epitope.

HXB2 Location gp160 (634–648)
Author Location gp41 (641–655 SF2)
Epitope EIDNYTNTIYTLLEE
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-A1, A2, B51, and B57.

HXB2 Location gp160 (678–686)
Author Location Env (679–687 subtype B)
Epitope WLWYIKIFI
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human (A2.1)
Keywords binding affinity
References Kundu *et al.* 1998a

- Ten HIV-1 + HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity.
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.

HXB2 Location gp160 (680–688)
Author Location gp41 (679–687 SF2)
Epitope WYIKIFIMI
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 1/4 HIV-1 + people tested.
- WYIKIFIFMI bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location gp160 (681–689)
Author Location Env (681–)
Epitope YIKIFIMIV
Epitope name Env681
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Env *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder, and induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.

HXB2 Location gp160 (685–693)
Author Location Env (686–694 subtype B)
Epitope FIMIVGGLV
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human (A2.1)
Keywords binding affinity
References Kundu *et al.* 1998a

- Ten HIV-1 + HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity.
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.

- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.
- ALTERNATIVE EPITOPE: IMIVGGLVGL – no CTL response was shown to the peptides FIMIVGGLV or IMIVGGLVGL.

HXB2 Location gp160 (698–707)
Author Location Env (696–706)
Epitope VFAVLSIVNR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*3303)
References Hossain *et al.* 2001; Takiguchi *et al.* 2000

- HLA-A33 a very common allele in Asian, with HLA-A*3303 the most common among the Japanese. New A*3303 epitopes were defined to better characterize the immune response in this population.
- The anchor motif for HLA*3303 (A, I, L, V, F, Y in position 2 (F and Y bind most strongly), and R (K is also tolerated) in the C-terminal position) was used to define 82 potentially reactive peptides in Env; 37/82 peptides bound to A*3303; 3/37 peptides could induce peptide-specific CTL in bulk PBMC cultures from 1/3 HLA A*3303 positive individuals tested.
- CTL clones were isolated that killed target cells in a concentration dependent manner after pulsing with the VFAVLSIVNR peptide, that could also kill cells transfected with env expressed from a vaccinia vector. Bulk cultures were tested from six additional people, and only 1/6 reacted with this peptide, but the peptide is in a highly variable region.

HXB2 Location gp160 (698–707)
Author Location gp41 (187–196)
Epitope VFAVLSIVNR
Immunogen HIV-1 infection
Species (MHC) human (A*3303)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (700–708)
Author Location Env (695–705 BH10, LAI)
Epitope AVLSVVNRV
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is LRIVFAVLSVV) has similarity with the human chemokine-factor 3 fragment LRLVFALVTAV .

HXB2 Location gp160 (700–708)
Author Location gp41 (705–714)
Epitope AVLSVVNRV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Ferris *et al.* 1999

- This epitope is processed by a TAP1/2 dependent mechanism.

HXB2 Location gp160 (701–719)
Author Location Env (691–710)
Epitope VLSIVNQVRRQGYSPLSFQT
Immunogen HIV-1 infection
Species (MHC) human (B15)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 5 epitopes from this individual that varied over time where the internal mutations became fixed; a dramatic decrease in CTL activity against the wild type epitope was observed as the mutation arose. The vlsivnKvrrqgysplsfqt variant found at 20 and 47 months postseroconversion.

HXB2 Location gp160 (701–720)
Author Location gp41 (701–720 BH10)
Epitope VLSIVNRVRQGYSPLSFQTH
Immunogen HIV-1 infection
Species (MHC) human (A32)
References Safrit *et al.* 1994a

- Recognized by CTL derived from acute seroconverter.

HXB2 Location gp160 (702–721)
Author Location Env (702–721)
Epitope LSIVNRVRQGYSPLSFQTLT
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location gp160 (704–712)
Author Location gp160 (704–712 LAI)
Epitope IVNRNRQGY
Subtype B
Immunogen
Species (MHC) human (A*3002)
Keywords optimal epitope
References Frahm *et al.* 2004; Goulder *et al.* 2001a

- C. Brander notes this is an A*3002 epitope.

HXB2 Location gp160 (704–712)
Author Location gp41
Epitope IVNRVRQGY
Epitope name IY9 (gp41)

Immunogen HIV-1 infection
Species (MHC) human (A*3002)
References Goulder *et al.* 2001a

- HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule.
- A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood.
- Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean.
- In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant.
- In subject 199 four additional A*3002 epitopes were identified.
- Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)

HXB2 Location gp160 (742–761)
Author Location Env (742–761)
Epitope RDRSIRLVSGFLALAWDDLR
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location gp160 (747–755)
Author Location gp41 (747–755)
Epitope RLVNGSLAL
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Parker *et al.* 1992

- Studied in the context of HLA-A2 peptide binding.

HXB2 Location gp160 (747–755)
Author Location gp41 (741–749 CM243 subtype CRF01)
Epitope RLVSGFLAL
Epitope name E747-755
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.

HXB2 Location gp160 (747–755)
Author Location gp41 (741–749 CM243 subtype CRF01)
Epitope RLVSGFLAL
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 2/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by two amino acids, RLVNGSLAL.
- This epitope was somewhat conserved 4/8 subtypes: CRF01 (E), B, C, and G.

HXB2 Location gp160 (754–768)
Author Location gp41 (SF2)
Epitope ALIWERDLRSLCLFSY
Epitope name Peptide78
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B22(55))
Assay type Chromium-release assay
References Carmichael *et al.* 1996

- Cross-reactivity of Env-specific CTL clones from 14 seropositive HIV-1 infected patients was tested using peptides based on 3 B clade variants (MN, IIIB, and RF). The proportion of CTL clones that cross-recognized conserved variants was low. Most CTL clones recognized only one peptide variant, indicating most Env responses are not cross-reactive within the B clade.
- This HLA B22(55) epitope was defined using SF2 peptides. The CTL clone that recognized it did not cross-recognize the MN, IIIB, or RF variants of this peptide.

HXB2 Location gp160 (754–768)
Author Location gp41
Epitope ALIWEDLRSLCLFSY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B55)
References Jin *et al.* 1998b

- Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction.

- Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK.

HXB2 Location gp160 (760–767)
Author Location gp41 (760–767)
Epitope LRSLFLFS
Immunogen HIV-1 infection
Species (MHC) human (A*2301)
Donor MHC A*2301, B*3501, B*1503 (B72), Cw2, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location gp160 (767–775)
Author Location gp41 (766–774 SF2)
Epitope SYRRLRDLL
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 1/4 HIV-1 + people tested.
- SYRRLRDLL bound to A*2402 moderately, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location gp160 (767–780)
Author Location gp41 (606–614 LAI)
Epitope SYHRLRDLLLIVTR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A31)
References Hammond *et al.* 1995

- Peptide only processed by a TAP-1/2-dependent pathway.
- CTL from an acute seroconverter.

HXB2 Location gp160 (769–777)
Author Location gp41 (769–777 BH10)
Epitope HRLRDLLLI
Immunogen HIV-1 infection
Species (MHC) human
References Safrit *et al.* 1994a

- Recognized by CTL derived from acute seroconverter.

HXB2 Location gp160 (770–778)
Author Location Env (679–777)
Epitope RLRDLLLIV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity
References Kmieciak *et al.* 1998a

- CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues.
- The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*.
- Peptides 5.3 and D2 bound to HLA A*0201 with low affinity.

HXB2 Location gp160 (770–780)
Author Location gp41 (775–785)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope that has been previously noted to be HLA A3.1, as well as seven others.

HXB2 Location gp160 (770–780)
Author Location gp41 (768–778 NL43)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
References Takahashi *et al.* 1991

- CD8+ T cell clone.

HXB2 Location gp160 (770–780)
Author Location gp41 (775–785 LAI)
Epitope RLRDLLLIVTR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0301 epitope.

HXB2 Location gp160 (770–780)
Author Location gp41 (770–780 BH10)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human (A*3101)
References Safrit *et al.* 1994a; Safrit *et al.* 1994b

- Recognized by CTL derived from acute seroconverter.
- C. Brander notes that this is an A*3101 epitope in the 1999 database.

HXB2 Location gp160 (770–780)
Author Location gp160 (770–780 LAI)
Epitope RLRDLLLIVTR
Subtype B
Immunogen
Species (MHC) human (A*3101)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*3002 epitope.

HXB2 Location gp160 (770–780)
Author Location gp41 (768–778 NL43)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords inter-clade comparisons
References Cao *et al.* 1997a

- The consensus peptide of clade B is RLRDLLLIVTR.
- The consensus peptide of clades A, C and E is RLRDFILIVTR and it is less reactive.
- The consensus peptide of clade D is SLRDLLLIVTR and it is less reactive.

HXB2 Location gp160 (770–780)
Author Location gp41 (775–785)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A3)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location gp160 (770–780)
Author Location gp41 (770–780)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.

HXB2 Location gp160 (770–780)
Author Location Nef (73–82)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.
- In two of the subjects, RLRDLLLIVTR was the dominant epitope.

HXB2 Location gp160 (770–780)
Author Location gp41 (769–780)
Epitope RLRDLLLIVTR
Epitope name A3-RR11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.

HXB2 Location gp160 (770–780)
Author Location Env (770–780)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human (A3)

Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 7 epitopes from this individual that varied over time, although the internal mutations did not become fixed. rlrdlllVItr variant residues were found. The V mutation arose at late time points, the I mutation arose at intermediate time points.

HXB2 Location gp160 (770–780)
Author Location Env (786–778)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 14 patients recognized this epitope.

HXB2 Location gp160 (770–780)
Author Location gp41 (770–780)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human (A31)
References Ferris *et al.* 1999; Hammond *et al.* 1995

- This epitope is processed by a TAP1/2 dependent mechanism.

HXB2 Location gp160 (770–780)
Author Location gp41 (770–780)
Epitope RLRDLLLIVTR
Immunogen HIV-1 infection
Species (MHC) human (A31)
Donor MHC A*0201, A31, B44, B60, Cw3, Cw16
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location gp160 (770–780)
Author Location Env
Epitope RLRDLLLIVTR
Epitope name TW10
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A31)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords epitope processing, escape
References Draenert *et al.* 2004b

- This study characterizes the N-terminal flanking position of the epitope ISPRTLNAW, and mutations in this position are thought to impact processing. The A31 epitope RLRDLLLIVTR was used as a negative control in this study.

HXB2 Location gp160 (777–785)
Author Location gp41 (782–790 LAI)
Epitope IVTRIVELL
Subtype B
Immunogen
Species (MHC) human (A*6802)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*6802 epitope.

HXB2 Location gp160 (781–802)
Author Location gp120 (788–809)
Epitope IVELLGRRGWEALKYWWNLLQY
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location gp160 (781–802)
Author Location gp41 (788–809 HXB2)
Epitope IVELLGRRGWEALKYWWNLLQY
Subtype B

Immunogen HIV-1 infection
Species (MHC) human (B27)
References Lieberman *et al.* 1992
- CTL epitope defined by T cell line and peptide mapping.

HXB2 Location gp160 (786–794)
Author Location gp41 (751–759)
Epitope GRRGWEALK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*2705)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004
- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- One of seven patients responded to this peptide with GzB producing cells, and a different patient responded with IFN-gamma producing cells.

HXB2 Location gp160 (786–794)
Author Location gp41 (791–799 LAI)
Epitope GRRGWEALK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords review
References McMichael & Walker 1994
- Review of HIV CTL epitopes.
- Also: J. Liebermann 1992 and pers. comm. J. Liebermann.

HXB2 Location gp160 (786–795)
Author Location gp41 (791–800 LAI)
Epitope GRRGWEALKY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*2705)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*2705 epitope.

HXB2 Location gp160 (786–795)
Author Location gp41 (791–800 LAI)
Epitope GRRGWEALKY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Lieberman 1998
- Optimal peptide mapped by titration J. Lieberman, pers. comm.

HXB2 Location gp160 (786–795)
Author Location gp41 (786–795)
Epitope GRRGWEALKY
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Day *et al.* 2001

HXB2 Location gp160 (787–795)
Author Location gp160 (787–795)
Epitope RRGWEVLKY
Immunogen HIV-1 infection
Species (MHC) human (A*0101)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (787–795)
Author Location gp41 (787–795)
Epitope RRGWEVLKY
Immunogen HIV-1 infection
Species (MHC) human (A1)
Donor MHC A1, A1, B8, B14, Cw7, Cw8
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003
- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location gp160 (794–802)
Author Location gp160 (794–802 LAI)
Epitope KYCWNLLQY
Subtype B
Immunogen
Species (MHC) human (A*3002)
Keywords optimal epitope
References Frahm *et al.* 2004; Goulder *et al.* 2001a
- C. Brander notes this is an A*3002 epitope.

HXB2 Location gp160 (794–802)
Author Location gp41
Epitope KYCWNLLQY
Epitope name KY9 (gp41)
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
References Goulder *et al.* 2001a

- HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule.
- A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood.
- Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean.
- In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant.
- In subject 199 four additional A*3002 epitopes were identified.
- Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)

HXB2 Location gp160 (794–802)
Author Location gp41 (283–291)
Epitope KYCWNLLQY
Immunogen HIV-1 infection
Species (MHC) human (A*3002)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (794–814)
Author Location gp41 (SF2)
Epitope KYCWNLLQYWSQELKNSAVSL
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.
- The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.

HXB2 Location gp160 (795–816)
Author Location gp41 (802–823 HXB2)
Epitope YWWNLLQYWSQELKNSAVNLLN
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1992

- CTL epitope defined by T cell line and peptide mapping.

HXB2 Location gp160 (799–807)
Author Location Env (800–808 subtype B)
Epitope LLQYWSQEL
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN
HIV component: gp160
Species (MHC) human (A2.1)
Keywords binding affinity
References Kundu *et al.* 1998a

- Ten HIV-1 + HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity.
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.

HXB2 Location gp160 (805–814)
Author Location Env (799–813 BH10, LAI)
Epitope QELKNSAVSL
Immunogen HIV-1 infection
Species (MHC) human
References Maksiutov *et al.* 2002

- This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is LLQYWSQELKNSAVS) has similarity with the complement component C6 fragment LTQFSSEELKNSGLT.
- This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is NSAVSLLNATAIAVA) also has similarity with the human INT-2 protooncogene protein precursor (fibroblast growth factor-3) fragment NSAYSILEITAVEVG.

HXB2 Location gp160 (805–814)
Author Location gp41 (810–819 LAI)
Epitope QELKNSAVSL
Subtype B
Immunogen
Species (MHC) human (B*4001)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4001,B60 epitope.

HXB2 Location gp160 (805–814)
Author Location gp41 (SF2)
Epitope QELKNSAVSL
Immunogen HIV-1 infection
Species (MHC) human (B60, B*4001)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes.
- B60 is present in 10-20% of the Caucasoid and very common in Asian populations.

HXB2 Location gp160 (805–814)
Author Location gp41 (805–814)
Epitope QELKNSAVSL
Immunogen HIV-1 infection
Species (MHC) human (B60, B61)
Keywords immunodominance
References Day *et al.* 2001

- No immunodominant responses were detected to five B61-restricted epitopes tested.

- All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response.

HXB2 Location gp160 (813–822)
Author Location gp41 (814–823 LAI)
Epitope SLLNATDIAV
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN
HIV component: gp160
Species (MHC) human (A*0201)
References Dupuis *et al.* 1995

- Of two CTL clones, one reacted only with 815-823, the other with 814-823 and 815-823.
- Noted to be A*0201 in Brander *et al.*, 1999 database.

HXB2 Location gp160 (813–822)
Author Location gp41 (818–827 LAI)
Epitope SLLNATDIAV
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN
HIV component: gp160
Species (MHC) human (A*0201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0201 epitope.

HXB2 Location gp160 (813–822)
Author Location gp41 (814–823)
Epitope SLLNATDIAV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords dendritic cells
References Kundu *et al.* 1998b

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients.
- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated.
- SLLNATDIAV is a conserved HLA-A2 epitope included in this study – 4/6 patients had this sequence as their HIV direct sequence, and 3 of these had a detectable CTL response – the other two had either the sequence SLFNAIDIAV or SLLNTTDIVV and no detectable CTL response.
- CTL demonstrated against peptide-coated target, epitope is naturally processed and enhancible with vaccine.

HXB2 Location gp160 (813–822)
Author Location gp41 (818–827)
Epitope SLLNATDIAV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes, including this epitope.

HXB2 Location gp160 (813–822)
Author Location gp41 (SF2)
Epitope SLLNATAIAV
Epitope name SV10
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords acute infection
References Goulder *et al.* 2001a

- Dominant CTL epitope in acute infection of patient AC13– response to this epitope corresponded to reduction of initial viremia.
- Several other subdominant CTL epitopes were identified in the acute phase, but a response to SL9, SLYNTVATL, was not evident until 18 months post-presentation.

HXB2 Location gp160 (813–822)
Author Location gp41 (77–85 SF2)
Epitope SLLNATDIAV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 2/6 group 2, and 1/4 group 3.

HXB2 Location gp160 (813–822)
Author Location gp41 (814–823 CM243 subtype CRF01)
Epitope SLLNATAIAV
Epitope name E813-82
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.

- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was reactive in HIV+ control study subjects 125 and 144 who carried HLA-A2.

HXB2 Location gp160 (813–822)
Author Location gp41 (814–823 CM243)
Epitope SLLNATAIAV
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by one amino acid, SLLNATDIAV.
- This epitope was somewhat conserved 4/8 subtypes: CRF01 (E), B, D, and F.

HXB2 Location gp160 (813–822)
Author Location gp41 (813–822)
Epitope SLLNATDIAV
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

HXB2 Location gp160 (813–822)
Author Location gp41 (813–822 IIIB)
Epitope SLLNATAIAV
Epitope name D2
Subtype B
Immunogen Vaccine
Vector/Type: DNA, DNA with protein boost *Strain:* B clade IIIB *HIV component:* gp160, gp160ΔV3 *Adjuvant:* IL-12
Species (MHC) mouse (A2)
Keywords vaccine-specific epitope characteristics
References Kiszka *et al.* 2002

- Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV.
- Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.

HXB2 Location gp160 (813–822)
Author Location Env (813–)
Epitope SLLNATDIAV
Epitope name Env813
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This epitope was one of the previously identified HLA-A2 epitopes studied.
- None of the 17 HIV-infected HLA-A2+ people in this study recognized this epitope.

HXB2 Location gp160 (813–822)
Author Location Env (814–823 subtype B)
Epitope SLLNATDIAV
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human (A2.1)
Keywords binding affinity
References Kundu *et al.* 1998a

- Ten HIV-1 + HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity.
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.
- CTL to overlapping peptides in this region gave a positive response in the greatest number of patients.

- ALTERNATIVE EPITOPES: LLNATDIAV and LLNATDIAVA – CTL were induced by vaccine in those that had the sequence SLLNATAIAVA in their own infection, but not in those with: NLLNTIAIAVA or NLFNTTAIAVA or SLLNATAITVA.

HXB2 Location gp160 (813–822)
Author Location gp41 (814–823 LAI)
Epitope SLLNATDIAV
Epitope name LR27
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG
Species (MHC) mouse (A2.1)
Keywords binding affinity, vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2001

- The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01).
- The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.
- HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants.
- All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.

HXB2 Location gp160 (813–822)
Author Location gp41 (814–823 LAI)
Epitope SLLNATDIAV
Epitope name LR27
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30
Species (MHC) mouse (A2.1)
Keywords vaccine-specific epitope characteristics, immunodominance
References Peter *et al.* 2002

- When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination Peter *et al.* [2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.

HXB2 Location gp160 (813–822)
Author Location gp41
Epitope SLLNATDIAV
Epitope name gp41 SV10
Immunogen HIV-1 infection
Species (MHC) human (A68)
Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- This epitope binds to three HLA-A2 supertype alleles: A*6802 (highest affinity), A*0202 and A*0203 (but not A*0201 and not A*0206)
- This epitope did not elicit an ELISPOT response in 22 chronic HIV HLA-A2 infections, but elicited a strong response in 1/12 acute HLA-A2 infections – this individual, AC13, was HLA A*0201/68 B44/14 and also had a strong response to HLA-A2 vpr epitope AIIRILQQL.

HXB2 Location gp160 (813–828)
Author Location gp41 (MN)
Epitope SLLNATAIAVAEGTDR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A2
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement, HAART, ART
References Chitnis *et al.* 2003

- 17 perinatally HIV-1 infected children (0.08-16 years) were evaluated for HLA-A2-restricted IFN-gamma CD8+ CTL responses against 4 immunodominant peptides that carry HLA-A2 epitopes. Two peptides were from gp120 (one at position 112, one from the V3 loop), and one each was from gp41 and Gag. 15/17 patients responded to the Gag peptide, 13/17 to the gp41 and the non-V3 gp120 peptides, and 11/17 responded to the V3 loop. 4 children recognized all 4 peptides.

HXB2 Location gp160 (814–822)
Author Location Env (815–823)
Epitope LLNATAIAV
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords binding affinity
References Kmieciak *et al.* 1998a

- CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL—all have A2 anchor residues.

- The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*.
- Peptides 5.3 and D2 bound to HLA A*0201 with low affinity and were variable, particularly D2.
- Substitutions in peptide D2: llnTIaiav did not abrogate the response, but diminished it.
- In a longitudinal study, the CTL response to the variable D2 epitope diminished over time, while the response to the conserved epitope D1 stayed higher.

HXB2 Location gp160 (814–822)
Author Location (C consensus)
Epitope LLDTIAIAV
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*0205)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location gp160 (814–822)
Author Location gp41 (815–823 LAI)
Epitope LLNATDIAV
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human (A2)
References Dupuis *et al.* 1995

- Of two CTL clones, one reacted only with 815-823, the other with 814-823 and 815-823.

HXB2 Location gp160 (814–822)
Author Location Env (815–823)
Epitope LLNATAIAV
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Kmieciak *et al.* 1998b

- Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length env gene product.

HXB2 Location gp160 (822–832)
Author Location gp41 (SF2)
Epitope VAEGTDRVIEI
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of individuals that had a CTL response to this epitope (HLA presenting molecule uncertain) broken down by group: 0 group 1, 1 group 2, and 0 group 3.

HXB2 Location gp160 (824–832)
Author Location gp160 (828–836 WEAU)
Epitope EGTDRIVIEI
Epitope name gp160 EI9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, acute infection, kinetics, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- This was one of five reasonably strong responses in early infection in the patient WEAU, and the epitope sequence did not vary during the first year of the infection.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Immunogen HIV-1 exposed seronegative

Species (MHC) human
References Pinto *et al.* 1995
- CTL and T helper cell reactivity in healthcare workers exposed to HIV.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Clerici *et al.* 1991a
- Helper and cytotoxic T cells can be stimulated by this peptide (Th4)

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{d, p, u, q}$)
References Shirai *et al.* 1992
- In a murine system multiple class I molecules can present to CTL.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (MHC) mouse (H-$2^{d, p, u, q}$)
References Shirai *et al.* 1996b
- Multiple murine MHC can cross-present this epitope (HP53), and P18 RIQRGPGRAFVTIGK, to specific CTL.

HXB2 Location gp160 (828–836)
Author Location gp41 (829–837 LAI)
Epitope RVIEVLQRA
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human (A2)
References Dupuis *et al.* 1995
- CTL from HLA-A2 positive subject react with this peptide.

HXB2 Location gp160 (828–836)
Author Location gp41 (829–837 CM243 subtype CRF01)
Epitope KVIEVAQGA
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Bond *et al.* 2001
- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by three amino acids, RvievLqRa.
- This epitope was only conserved in CRF01 (subtype E), and identities were rare.

HXB2 Location gp160 (828–836)
Author Location Env (829–837 subtype B)
Epitope RVIEVLQRA
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human (A2.1)
Keywords binding affinity
References Kundu *et al.* 1998a
- Ten HIV-1 + HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity.
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.
- CTL responses after reimmunization may include recall responses – individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.

HXB2 Location gp160 (830–854)
Author Location gp41 (831–853)
Epitope IEVVQGAYRAIIRHIPRRIRQGLERI
Immunogen HIV-1 infection
Species (MHC) human
References Price *et al.* 1995
- Study of cytokines released by HIV-1 specific activated CTL.

HXB2 Location gp160 (831–838)
Author Location Env (830–837)
Epitope EVAQRAYR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*3303)
References Hossain *et al.* 2001; Takiguchi *et al.* 2000
- HLA-A33 a very common allele in Asia, with HLA-A*3303 the most common among the Japanese. New A*3303 epitopes were defined to better characterize the immune response in this population.
- The anchor motif for HLA*3303 (A, I, L, V, F, Y in position 2 (F and Y bind most strongly), and R (K is also tolerated) in the C-terminal position) was used to define 82 potentially reactive peptides in Env; 37/82 peptides bound to A*3303; 3/37 peptides could induce peptide-specific CTL in bulk PBMC cultures from 1/3 HLA A*3303 positive individuals tested.
- 2/3 peptides that reacted with the bulk culture, EVAQRAYR and VIEVAQRAYR, were overlapping, with one encompassing the other, but EVAQRAYR was shown to be the one that was reactive with a CTL clone.

- CTL clones were isolated that killed target cells in a concentration dependent manner after pulsing with the EVAQRAYR peptide, that could also kill cells transfected with env expressed from a vaccinia vector. Bulk cultures were tested from six additional people, and only 2/6 reacted with this peptide, but the peptide is in a highly variable region.

HXB2 Location gp160 (831–838)
Author Location gp41 (320–327)
Epitope EVAQRAYR
Immunogen HIV-1 infection
Species (MHC) human (A*3303)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (833–841)
Author Location gp160 (837–845 WEAU)
Epitope VQRTCRAIL
Epitope name gp160 VL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A*2902, B*4403, B*0801
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords dynamics, immunodominance, acute infection, characterizing CD8+ T cell responses, reversion, viral fitness
References Jones *et al.* 2004

- Primary CD8+ T-cell response to Env, Tat and Gag and the extent, kinetics and mechanisms of viral escape were examined in three patients. Rapid escape,within weeks from infection, from HIV specific CTL responses was observed in all three patients, but the kinetics and extent of the escape differed depending on the breadth and co-dominant distribution of CTL-mediated pressure. The two patients that rapidly declined had more focused immunodominant responses, while the single patient that had low viral load and stable CD4 counts for seven years had a broad co-dominant response and less escape.
- The patient WEAU had high viral loads and rapid CD4 decline. WEAU mounted 14 detected CTL responses, with distinct patterns of immunodominance. WEAU did not control viral replication well, and escape mutations occurred early and 4/14 had changes that could have resulted in escape, and two were confirmed as escape.
- This was one of five reasonably strong responses in early infection in the patient WEAU, and the epitope sequence did not vary during the first year of the infection.

HXB2 Location gp160 (835–843)
Author Location Env (834–842 SF2)
Epitope RAYRAILHI
Immunogen HIV-1 infection
Species (MHC) human (B*5101)
Keywords rate of progression
References Tomiyama *et al.* 1999

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed.
- This peptide could stimulate CTL from one person, however this CTL clone did not recognize B*5101 positive target cells infected with HIV-1 recombinant vaccinia expressing Env, so it was not confirmed that this peptide was a properly processed epitope.

HXB2 Location gp160 (835–843)
Author Location Env (835–843)
Epitope RAYRAILHI
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 7 epitopes from this individual that varied over time, although the internal mutations did not become fixed. The rTFrailhi variant residues arose at early time points, rIyrailhX variant residues arose at intermediate time points.

HXB2 Location gp160 (837–856)
Author Location gp120 (844–863)
Epitope YRAIRHIPRRIRQGLERILL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location gp160 (837–856)
Author Location gp120 (844–863 SF2)
Epitope YRAIRHIPRRIRQGLERILL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-A2, A26, B7, and B38.

HXB2 Location gp160 (837–856)
Author Location gp120 (844–863 LAI)
Epitope YRAIRHIPRRIRQGLERILL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Shankar *et al.* 1996

HXB2 Location gp160 (837–856)
Author Location gp41 (844–863 HXB2)
Epitope YRAIRHIPRRIRQGLERILL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Lieberman *et al.* 1992
- CTL epitope defined by T cell line and peptide mapping.

HXB2 Location gp160 (842–856)
Author Location gp41 (SF2)
Epitope HIPRRIRQGLERALL
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2001a
- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- The only Env peptide recognized was gp41 HIPRRIRQGLERALL.

HXB2 Location gp160 (843–851)
Author Location gp41 (848–856 LAI)
Epitope IPRRIRQGL
Subtype B
Immunogen
Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*0702 epitope.

HXB2 Location gp160 (843–851)
Author Location gp41 (848–856 LAI)
Epitope IPRRIRQGL
Subtype B
Immunogen
Species (MHC) human (B7)
Keywords mother-to-infant transmission
References Brander & Walker 1995
- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.

HXB2 Location gp160 (843–851)
Author Location
Epitope IPRRIRQGL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords immunodominance, escape
References Soudeyns *et al.* 1999
- Following primary infection, progressive diversification and accumulation of mutations of HIV-env nucleotide sequences was observed, focused in V2 in one individual and in V8 in another.
- The patient with the V2 diversification showed only transient CTL against Env and Nef.
- The patient with the V8 diversification had an immunodominant CTL response to V8 epitope IPRRIRQGL, and multiple escape variants emerged within a year: ipTrirqgl and ipTrirqgF, which abrogated the CTL response *in vitro*, and also iprrLqgl and iprrirqDl which gave diminished responses.

HXB2 Location gp160 (843–851)
Author Location gp41 (848–856 LAI)
Epitope IPRRIRQGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords inter-clade comparisons
References Cao *et al.* 1997a
- The consensus peptide of clades A, B, D, and F is IPRRIRQGL.
- The consensus peptide of clade C is iprrirqgF, and it is equally reactive.

HXB2 Location gp160 (843–851)
Author Location gp41 (848–856 subtype B)
Epitope IPRRIRQGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords inter-clade comparisons, acute infection
References Wilson *et al.* 1998b
- The extent of CTL interclade cross-reactivity from CTL isolated from individuals newly infected with B clade virus was studied, and extensive cross-reactivity was observed.
- Two HLA B7 individuals had CTL response to B_LAI, A_92UG037 and C_92BR025 gp160, but were B clade strain MN non-responders – the authors note that the B7 epitope IPRRIRQGL is conserved between the LAI and clade A and C strains, but that MN has a non-conservative Arg to Thr substitution at position three that may be contributing to the specificity of the response in the HLA B7 individuals.

HXB2 Location gp160 (843–851)
Author Location gp41 (843–851 HXB2)
Epitope IPRRIRQGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, immunodominance
References Hay *et al.* 1999
- CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201.
- The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted.

- Despite the initial narrow response to two epitopes, no other CTL responses developed.
- No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak.
- Variants were observed *in vivo*, the most common form of the viral epitope at presentation at 3 months was the only form that did not elicit a CTL response: iprrTrqgl; the other forms detected were iprrirqgF, iprriLqgF, VprrirqgF and they could elicit a CTL response although the response to iprriLqgF was reduced.
- A second rapid progressor had a detectable CTL response exclusively to this epitope.

HXB2 Location gp160 (843–851)
Author Location gp41 (subtype A)
Epitope IPRRIRQGF
Subtype A
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords inter-clade comparisons
References Cao *et al.* 2000

- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D.
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.
- This optimal epitope sequence, recognized by CTL derived from a Ugandan with an A subtype infection, is cross-reactive with subtypes A and B, but not in subtype D.

HXB2 Location gp160 (843–851)
Author Location gp41
Epitope IPRRIRQGL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Islam *et al.* 2001

- Subject 053i was followed longitudinally from acute infection through death, and had rapid progression to AIDS.
- This individual had a dominant response to IPRRIRQGL with strong *in vivo* activated responses and *in vitro* stimulated memory responses and a subdominant response to SPAIFQSSM – during the course of disease progression (4 Years), the functional CTL responses were lost and no sequence variation occurred with in both epitopes.
- At 3 months post-presentation, seven IPRRIRQGL CTL clones were obtained, five used the T-cell receptor Vβ 6S1 and Jβ 2.7 and had the CDR3 WAASS, two used Vβ16S1, ERSPPGD, Jβ 2.7 and one CTL clone isolated at 39 months was Vβ 14S1, CR3 PTAAG, and Jβ 2.1 – all of these clones persisted over the course of the infection, even to time of death, despite the loss of CTL functional responses over time.

HXB2 Location gp160 (843–851)
Author Location gp41 (843–851 SF2)
Epitope IPRRIRQGL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 2/4 group 1, 1/3 group 2, and 1/1 group 3.

HXB2 Location gp160 (843–851)
Author Location gp41 (848–856)
Epitope IPRRIRQGL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B7)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- IPRRIRQGL cross-reacts with clades A, B and D.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B7 women, 2/5 HEPS and 5/6 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in 2 of the 5/6 HIV-1 infected women that responded to the epitope, but in neither of the 2/5 HEPS cases.
- Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGV/IRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.

HXB2 Location gp160 (843–851)
Author Location gp41 (843–851)
Epitope IPRRIRQGL
Immunogen HIV-1 infection

Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location gp160 (843–851)
Author Location gp41 (SF2)
Epitope IPRRIRQGL
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.

HXB2 Location gp160 (843–851)
Author Location gp41 (842–852)
Epitope IPRRIRQGL
Epitope name B7-IL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), immunodominance, acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- Only two epitopes were detected during acute infection in patient AC-06, B7 restricted gp41 epitope IPRRIRQGL and Gag GPGHKARVL. GPGHKARVL was the first targeted peptide, and remained immunodominant through the 34 month study period.
- 6/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.

HXB2 Location gp160 (843–851)
Author Location gp41
Epitope IPRRIRQGL
Epitope name B7-IL9(gp41)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A24, A?, B7, B27
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).

HXB2 Location gp160 (843–851)
Author Location Env
Epitope IPRRIRQGL
Epitope name EW10
Immunogen HIV-1 infection
Species (MHC) human (B7)
Assay type Chromium-release assay, Flow cytometric CTL assay
Keywords class I down-regulation by Nef
References Bobbitt *et al.* 2003

- Nef, through Nef-mediated MHC-1 down-regulation, is not the only viral protein to influence levels of HIV-specific CTL recognition. The Rev L60F mutation, a common natural variant, can decrease CTL recognition of late gene products. The Rev mutation impacts the early to late gene switch, reducing late gene product production (Gag, Pol, Env, Vpu, Vpr and Vif), while increasing Nef production, both of which reduce the

impact CTL recognition of late gene products. As expected, Rev L60F rendered HIV infected cells more resistant to CTL that recognized epitopes from the late proteins Env and Gag. Gag expression is reduced more than Env, and Gag-specific CTL were more profoundly affected. Conversely CTL against an epitope in an early gene product, Tat, were more effeciently recognized when infected with viruses carrying the Rev L60F mutation.
- Patients in the asymptomic phase with active immune responses had more CTL resistant viruses, with lower Rev activity, lower Gag expression and greater resistance to Gag-specific CTL killing, while viruses isolated from people with AIDS were more sensitive to CTL killing.

HXB2 Location gp160 (843–851)
Author Location gp41 (843–851)
Epitope IPRRIRQGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A1, A3, B7, B14, Cw*0702, Cw*0802
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location gp160 (843–851)
Author Location gp41
Epitope IPRRIRQGL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- 3/9 HLA B7+ infection-resistant men, compared to 0/4 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location gp160 (843–851)
Author Location Env (333–341)
Epitope IPRRRIRQGL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 3/7 patients recognized this epitope.

HXB2 Location gp160 (843–851)
Author Location (B consensus)
Epitope IPRRIRQGL
Epitope name IL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A31, A68, B07, B70, Cw7, Cw1
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location gp160 (843–851)
Author Location gp41
Epitope IPRRIRQGL
Subtype B
Immunogen HIV-1 infection

Species (MHC) human (B7)
Country United Kingdom.
Assay type Tetramer binding, T-cell Elispot, Intracellular cytokine staining
Keywords rate of progression, acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Papagno *et al.* 2004

- Acute HIV-1 infection induces massive activation of HIV-specific and non-HIV-specific CD8+ T-cells resulting in differentiation of these cells. High differentiation of CD8+ T-cells is correlated with disease progression. Differentiation is a natural process but it can be driven by elevated immune activation, such as in HIV infection.

HXB2 Location gp160 (843–851)
Author Location gp41 (333–334)
Epitope IPRRIRQGL
Epitope name IPR
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This was one of 8 reactive epitopes found not to vary over time.

HXB2 Location gp160 (845–856)
Author Location gp41 (852–863 HXB2)
Epitope RRIRQGLERILL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A30, B8)
References Lieberman *et al.* 1992

- CTL epitope defined by T cell line and peptide mapping.

HXB2 Location gp160 (845–856)
Author Location gp41 (852–863 LAI)
Epitope RRIRQGLERILL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Shankar *et al.* 1996

HXB2 Location gp160 (846–854)
Author Location
Epitope RIRQGLERA
Epitope name Env-RA9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0205)
Donor MHC A*0205 A*3002 B*1402 B*5301 Cw*0401 Cw*0802
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- This epitope was newly defined in this study.
- Patient 00RCH28 was African American, not on HAART, had a viral load of 5900 and CD4 count of 889, and she also recognized IN(219-227), KIQNFRVYY, A*3002.
- Among HIV+ individuals who carried HLA A02, 6/21 (29%) recognized this epitope.

HXB2 Location gp160 (846–854)
Author Location gp41 (335–343)
Epitope RIRQGLERA
Immunogen HIV-1 infection
Species (MHC) human (A*0205)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location gp160 (849–856)
Author Location gp41 (849–856)
Epitope QGLERALL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A1, A1, B8, B14, Cw7, Cw8
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.

- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

II-B-20 Env CTL, CD8+, epitopes

HXB2 Location Env
Author Location gp160 (LAI, MN)
Epitope
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Protease
Species (MHC) human
References Belshe *et al.* 1998

- The live canarypox vaccine ALVAC-HIV(vCP205) carrying MN gp120, LAI gp41, Gag and Protease, and boosted with SF-2 rpg120, was given to HIV-1 seronegative volunteers – HIV-specific Env or Gag CD8+ CTL were detected in 64% of the volunteers.

HXB2 Location Env
Author Location gp160 (LAV)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, dendritic cells
References Zheng *et al.* 1999

- Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone.
- Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway.

HXB2 Location Env
Author Location Env (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1
References Wasik *et al.* 2000

- HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of IL-2, as well as beta-chemokines, relative to other HIV+ infants.
- No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors.
- CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Soudeyns *et al.* 2000

- Analysis of T cell receptor beta chain variable region repertoire indicates that antiretroviral therapy (ART) and highly active antiretroviral therapy (HAART) decrease global CD8 T cell oligoclonality during primary HIV infection.
- A sharp decline in HIV-1 gp120-specific CTL clones was observed in HAART-treated subjects.

HXB2 Location Env
Author Location Env (LAI, MN)
Epitope
Immunogen Vaccine
Vector/Type: canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp41, Protease, V3
Species (MHC) human
References Salmon-Ceron *et al.* 1999

- The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36))
- Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36.
- Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords TCR usage
References Gamberg *et al.* 1999

- 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL *in vitro*, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens.
- Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR betaV gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases.

HXB2 Location Env
Author Location Env (LAI, MN)
Epitope
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade LAI, B clade SF2 *HIV component:* Env, Gag, Nef, Protease
Species (MHC) human
References Gorse *et al.* 1999b

- The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120.

- In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients.
- The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity.

HXB2 Location Env
Author Location Env (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Buseyne *et al.* 1998b

- In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes.

HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* gp120, gp160
Species (MHC) macaque
References Shiver *et al.* 1997

- DNA vaccinations of Rhesus monkeys with a gp120 or gp160 DNA vaccine elicited a strong CD8 cytotoxic T cell response.

HXB2 Location Env
Author Location gp160
Epitope
Immunogen HIV-1 infection
Species (MHC) macaque
References Kent *et al.* 1997b

- Macaques can be infected with HIV, and clear the infection within 6 months, so it is of interest to examine their initial immune response.
- A strong CTL response against env, pol and gag antigens can be detected.
- The CTL response peaked by 4 weeks and declined dramatically by 8 weeks.
- The response in the lymph nodes and peripheral blood was comparable.

HXB2 Location Env
Author Location gp160
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12
Species (MHC) mouse
References Kim *et al.* 1997c

- A gag/pol, vif or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice.
- When IL-12 was present, CTL response could be detected even without *in vitro* stimulation.

HXB2 Location Env
Author Location gp160
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12
Species (MHC) mouse
References Kim *et al.* 1997d

- A gag/pol or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules CD86, gave a dramatic increase in both the cytotoxic and proliferative responses in mice.
- When CD86 was present, CTL response could be detected even without *in vitro* stimulation.

HXB2 Location Env
Author Location gp120 (HXBc2)
Epitope
Immunogen Vaccine
Vector/Type: DNA prime with gp160 boost *Strain:* B clade HXBc2 *HIV component:* gp160
Species (MHC) macaque
References Letvin *et al.* 1997

- Vaccination of Macaques mulatta (Rhesus monkeys) with an HXBc2 env DNA prime and a protein boost elicited a T cell proliferative response, a CTL response, and type-specific neutralizing antibodies.
- Vaccinated animals challenged with SHIV-HXB2 were protected from infection.

HXB2 Location Env
Author Location gp120 (MN)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade MN *HIV component:* Env, Rev
Species (MHC) human
References MacGregor *et al.* 1998

- An HIV DNA env and rev vaccine given to 15 asymptomatic HIV+ individuals at three different dosages, 30, 100 or 300 ug, was safe.
- The CTL response to gp120 was enhanced in 0/4 patients in the 30 μg group, 2/3 patients in the 100 μg group, and 0/3 in the 300 μg group – but the non-responding patients in the 300 μg group had a strong CTL response prior to vaccination, and the CTL results are inconclusive.

HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Trickett *et al.* 1998

- Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection.
- Improvement in CD4+ and CD8+ T cells was seen in 7/12, and an increase in the CTL response to Env was seen in one patient.

HXB2 Location Env
Author Location gp120 (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Legrand *et al.* 1997

- Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat.
- An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef.
- Early responses to Pol, Rev, Vif and Tat were rare.

HXB2 Location Env
Author Location gp120 (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* gp160
Species (MHC) human
References Corey *et al.* 1998

- Vaccinia-naive subjects were vaccinated with vaccinia-gp160 LAI and boosted with gp120 SF2, LAI, MN, or 160 MN.
- 26/51 had an anti-Env CTL response, and those that were boosted with gp120 tended to produce Abs that neutralized autologous laboratory strains with some cross-reactivity.

HXB2 Location Env
Author Location Env (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Betts *et al.* 1997

- 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins.
- A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References De Maria *et al.* 1997

- CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function.
- Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels.

HXB2 Location Env
Author Location Env (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Betts *et al.* 1999

- This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection.

HXB2 Location Env
Author Location Env (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Buseyne *et al.* 1998a

- This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human
References Goh *et al.* 1999

- 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype.
- In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins.

HXB2 Location Env
Author Location Env (LAI, MN)
Epitope
Immunogen Vaccine
Vector/Type: canarypox *HIV component:* Gag, gp120, gp41, Nef, Protease, RT
Species (MHC) human
References Evans *et al.* 1999

- A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination.

HXB2 Location Env
Author Location Env (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA prime with vaccinia boost *Strain:* B clade LAI *HIV component:* Env, Gag
Species (MHC) macaque
Keywords Th1, Th2
References Kent *et al.* 1998

- Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T cell immunity than either vaccine alone.
- The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced.

HXB2 Location Env
Author Location Env (LAI, MN)
Epitope
Immunogen Vaccine
Vector/Type: canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease
Species (MHC) human
References Salmon-Ceron *et al.* 1999

- A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy, uninfected volunteers.

HXB2 Location Env
Author Location Env (MN)
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86
Species (MHC) chimpanzee
References Kim *et al.* 1998

- The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.

HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Immunogen Vaccine
Vector/Type: Semliki-Forest Virus with virus-like particle boost *Strain:* B clade IIIB *HIV component:* Gag, gp120
Species (MHC) macaque
References Notka *et al.* 1999

- Immunization of SIV Pr56Gag-derived VLPs with HIV-1 gp120 anchored on their surface induced Abs, CTL and Th responses to HIV gp120; priming with the HIV antigens in Semliki-Forest Viruses enhanced the immunological outcome.
- Immunized monkeys challenged with SHIV showed a more rapid reduction of plasma viremia.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human
References Akridge *et al.* 1999

- This study suggests that HIV-1-resistance in exposed and uninfected individuals is not only associated with the 32-bp deletion in the HIV-1 co-receptor CCR5, but can be related to HIV-1 specific CTL immunity.

HXB2 Location Env
Author Location gp120 (BRU)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Aladdin *et al.* 1999

- In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Aladdin *et al.* 2000

- The administration of IL-2 caused an initial enhancement of CD4 cell counts that was accompanied by a decrease in CTL activity – IL-2 therapy did not reduce initial HIV viral load and viral replication was ultimately enhanced.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Jin *et al.* 1998a

- CTL precursor frequencies were determined in HIV-1 infected pregnant women, and higher CTLp frequencies to Pol and SF2 Nef, but not IIIB Nef, were found in non-transmitting mothers than in transmitting mothers – Nef CTL responses have been found in uninfected infants born to HIV+ women (Lazuriaga95);
- Very different CTLp frequencies were observed in env depending on whether IIIB, MN, RF, BK, or SF2 was used as antigen – no association between env specific CTL and transmission was observed.

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* Env
Species (MHC)
Keywords review
References Zavala *et al.* 2001

- This paper is a review of vaccinia in the context of vaccines strategies that use different vectors to prime and boost, and emphasizes a unique capacity of vaccinia to very efficiently boost memory T-cell responses.

- HIV is discussed in the context of Gonazalo *et al.* 1999, where a V3 CTL epitope expressed in reFlu was boosted most effectively by vaccinia expressing the full Env.

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* ZF1 *HIV component:* complete genome
Species (MHC) macaque
References Akahata *et al.* 2000

- Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging.
- Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153)
- 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected.
- PBMC from all vaccinated monkeys produced IFN-gamma, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response.
- 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit.
- 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Young *et al.* 2001

- Addition of recombinant rec human IL12 (rhIL12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/ul > 500.
- 2/10 individuals with <200 CD4 cells/ul, and 3/10 individuals with 200-500 CD4cells/ul, had an increase of >5% upon treatment of the culture with rhIL12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL12.

HXB2 Location Env
Author Location Env (subtype A, B, D)
Epitope
Subtype A, B, D
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Cao *et al.* 2000

- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D.
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine
Vector/Type: canarypox, protein *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Env, Gag, Protease *Adjuvant:* MF59
Species (MHC) human
References AVEG022PT 2001

- Different HIV strains were used for different regions: MN (gp120), LAI (gp120, protease and gag), and SF2 gp120
- 26/42 subjects who received CP vac-env-pro vaccine had a CTL response measured by Cr-release, while only 3/17 who were vaccinated with rec gp120 had a CTL response.
- A combination of a CP vac-env-pro vaccine with rec gp120 gave CD8+ T-cells in 62% of subjects, and NAbs in 91% of subjects.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References White *et al.* 2001

- HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women.

HXB2 Location Env
Author Location Env (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Jin *et al.* 2000a

- The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets.
- LTNPs have high memory CTL numbers and low viral load.

HXB2 Location Env
Author Location Env (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human

Keywords HAART, ART, rate of progression
References Jin *et al.* 2000a

- The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay.
- LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Keywords review, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 2001

- This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population.
- The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays.
- CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases.
- CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response.
- HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people.

HXB2 Location Env
Author Location
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol
Species (MHC) mouse
Keywords review
References Nabel 2002

- Env DNA constructs were designed that were codon optimized for human genes, express Env in the absence of the regulatory protein Rev, both increasing Env expression levels, deletions in the cleavage site and in the fusion domain. These constructs increased Ab responses to Env, while not diminishing CTL responses, when injected into mice.
- Removing N-linked glycosylation sites did not alter the humoral or cellular immune responses to this HIV protein, as has been seen in analogous SIV experiments.

HXB2 Location Env
Author Location
Epitope
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References De Maria *et al.* 1994; Kuhn *et al.* 2002

- 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Env
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission, rate of progression
References Kuhn *et al.* 2002; Wasik *et al.* 1999

- In HIV-infected infants HIV-specific, CTL responses were not detectable in cord blood or in PBMC collected shortly after birth and were absent or remained very low in 3 infants with a rapidly progressive disease. For those who progressed more slowly, the HIV-specific CTL activity varied.
- The two infants with high levels of Env peptide-stimulated IL-2 responses had the highest CTLp frequencies.
- Stronger responses were detected after initiation of the antiretroviral therapy.
- Two babies that were not infected though born to HIV+ mothers had detectable though low HIV-specific CTLp responses to Env (1/2), Pol (2/2), Gag (1/2) cord blood and transiently in PBMC after birth.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Env
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References Aldhous *et al.* 1994; Kuhn *et al.* 2002

- Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points.

- Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses Tat (1/2), Pol (2/2), Gag (1/2).
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Env
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References Kuhn *et al.* 2002; McFarland *et al.* 1994

- Only 9% of HIV+ infants had HIV-specific CTL against Env or Gag in unstimulated PBMC. After CD3 stimulation of PBMC, Gag and Env specific CTL were found in PBMC from 91% and 78% of HIV-infected children, respectively, with high precursor frequencies.
- 2/9 babies that were not infected though born to HIV+ mothers had detectable responses to Env.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Env
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.

HXB2 Location Env
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Trabattoni *et al.* 2002

- CD8+ T-cells that were stimulated by HIV-1 Env expressing targets from 25 HIV+ patients receiving ART and 17 ART-naive patients were compared. CTL from the individuals receiving ART showed increased TNFalpha production and a reduction of perforin and granzyme expressing CTL, suggesting a functional defect in ART-treated individuals, and a potential benefit of immunomodulants during therapy.

HXB2 Location Env
Author Location (HXB2)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Edwards *et al.* 2002

- 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag.
- Nef and/or Pol CTL responses were detected in 86% of the subjects.
- The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load.
- Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count.
- Nef and Env responses did not correlate with either CD4 counts or viral load.

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* cationic liposome, GM-CSF, IL-2
Species (MHC) mouse
Keywords Th2
References Ishii *et al.* 2001

- Vaccination route of HIV-1 DNA immunization with gp160 and Rev genes was compared including intranasal (i.n.), intramuscular (i.m.), and topical application of DNA directly on the skin after elimination of keratinocyte layers using a strong adhesive. Topical exposure resulted in high level CTL responses, IFN-gamma and IL-4 production, and delayed type hypersensitivity (DTH). Topical application favored Th2 responses.
- DNA delivered topically with adjuvant-like cationic liposomes gave a stronger response than DNA alone, and co-administration of the DNA vaccine with IL-12 and GM-CSF expression vectors enhanced cytotoxic activity and DTH.

HXB2 Location Env
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, dendritic cells
References Larsson *et al.* 2002b

- Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.

HXB2 Location Env
Author Location (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunotherapy
References Trickett *et al.* 2002

- Conditions were optimized for ex-vivo expansion of CD8+ and CD4+ T-cells with the goal of functional T-cell production for autologous immunotherapy. 10,000-fold expansions were obtained in 14 days with optimized concentrations of IL-2, anti-CD3 and anti-CD28 coated microspheres, and decreasing amounts of serum over the first 8 days.

HXB2 Location Env
Author Location (IIIB)
Epitope
Subtype B
Immunogen HIV-1 and HCV co-infection
Species (MHC) human
Keywords rate of progression
References Lauer *et al.* 2002

- HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins.
- All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load.
- Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted.
- HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.

HXB2 Location Env
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords responses in children
References Luzuriaga *et al.* 1995

- 2/3 infants infected in utero had detectable HIV-1 Gag and Env specific CTL responses, one by 4 months, one by 11 months of age. Levels of the responses varied at different time point. Pol responses were not detected.
- 2/4 infants infected intrapartum had detectable responses, one note until 11 months, one not until 42 months.
- HIV-specific CTL were not detected in ten HIV- infants that were born to HIV+ mothers.

HXB2 Location Env
Author Location
Epitope
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *HIV component:* Env, Gag
Species (MHC) human
References Gupta *et al.* 2002

- A safety and immunogeniticity study of a vaccine dosing schedule was studied in a trial conducted in high and low risk study subjects. There was a 76% cumulative probability of detecting a Gag or Env CTL response by day 728.

HXB2 Location Env
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, responses in children
References Scott *et al.* 2001

- CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age.
- Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses.
- One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol.
- Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.

HXB2 Location Env
Author Location (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, supervised treatment interruptions (STI)
References Ortiz *et al.* 2001

- Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.

- One of seven subjects with a detectable NAb response had an augmented neutralization titer in response to STI.

HXB2 Location Env
Author Location (SF2)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC B*3501, A*2402, B*5101, B*3303
Keywords class I down-regulation by Nef
References Tomiyama *et al.* 2002

- Nef down-regulates class I molecules, and the killing activity of HLA B*3501, A*2402, B*5101 and B*3303-restricted HIV-1-epitope specific CTL clones was inhibited by an HIV-1 strain carrying Nef, relative to a Nef-deleted virus; while Nef-induced HLA class I down-regulation inhibited lysis, it did not abolish cytokine production by HIV-1-specific CD8+ T-cells.

HXB2 Location Env
Author Location Env (gp160) (IIIB)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade NL43 *HIV component:* Env
Species (MHC) macaque
References Akahata *et al.* 2003

- Four monkeys were injected i.m. with a SHIV plasmid (SHIV-NM-3rn ZF1*) which encodes all viral proteins driven by the SIV LTR promoter. Infectivity is prevented by the introduction of mutations within the zinc-finger motifs of the nucleocapsid (NC) that prevents RNA packaging. An original NC ZF1 mutant plasmid was constructed using NL43 (Akahata 275:116-124 (2000) – the SHIV construct was made as an alternative to get improved expression in macaques using an SIV promotor. CTL were detected by lysis of HIV-1 Env IIIB or SIV Gag mac239 expressing expressing target cells, and a T cell proliferative response to Env was observed. Env-directed antibodies were detected by ELISA. All vaccinated macaques had a low peak viral loads that fell below the level of detection within 6 weeks post-challenge with autologous SHIV SHIV-NM-3rn.

HXB2 Location Env
Author Location Env (MN)
Epitope
Subtype B
Immunogen SIV infection, SHIV infection
Species (MHC) macaque
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement
References Calarota *et al.* 2003

- The senstitivity of gamma INF Elispot assays can be enhanced for the detection of low frequency responses, like after ART, by adding IL-15 to the assay.
- CD8+ T-cells from SHIV and SIV infected macaques with peptide pools from Gag and Env were used to test this system.

HXB2 Location Env
Author Location Env
Epitope
Subtype multiple
Immunogen
Species (MHC) human
Assay type Flow cytometric CTL assay
Keywords inter-clade comparisons
References Currier *et al.* 2003

- CD8-cellular immune responses from 21 HIV-1 infected patients from Kenya infected with subtype A, C, D, and unique recombinants were studied for cross-recognition of Gag, Env, and Nef vaccinia-expressed proteins representing subtypes A-H, including CRF01.
- Both subtype-specific and cross-reactive CTL were observed, with a skewing of responses towards the infecting subtype in the nine subjects with full length sequence available. The magnitude of the responses to Gag were the highest, less to Nef, and still less to Env.
- For Gag, 8/21 subjects responded to at least 7/8 different subtype proteins, 7 had a mixed response, recognizing some subtypes but not others, and 6 responded to only one or none of the different subtype proteins. For Env, 4/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 7 responded to one or none. For Nef, 5/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 6 responded to one or none.

HXB2 Location Env
Author Location Env (HIV-1 IIIB)
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Assay type cytokine production
Keywords HIV exposed persistently seronegative (HEPS)
References Fowke *et al.* 2000

- A cohort of Nairobi sex-workers were defined as resistant to HIV-infection by virtue of remaining seronegative despite repeated high risk exposures. 24 were tested for HIV specific T-helper responses detemined by IL-2 production *in vitro* in response to gp120 peptides or soluble gp120 protein.
- 7/17 resistant women showed IL-2 stimulation which was greater than or equal to 2.0, and specific CTL responses were detected in 15/22 resistant women as compared to 0/12 of the control low-risk subjects.

HXB2 Location Env
Author Location gp160 (MN)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade MN *HIV component:* gp160 *Adjuvant:* IL-12
Species (MHC) mouse
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords adjuvant comparison
References Chattergoon *et al.* 2004

- pIL-12 used as adjuvant is shown to significantly increase the numbers of Ag-specific CD8+ T-cells and a sustained memory response. Also, the splenocytes from mice that recieved pIL-12 were shown to proliferate to a much higher extent. Mice immunized with a plasmid expressing the influenza A/PR8/34 HA gene and pIL-12 were shown to be better able to control the infection.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, Flow cytometric CTL assay
Keywords HAART, ART, immune dysfunction
References Trabattoni *et al.* 2004

- Reduced perforin-and granzyme- containing Env-specific CD8+ T cells were observed in ART treated individuals indicating that antiretroviral drugs might directly interfere with the production of perforin and granzymes, inhibiting CTL killing. Immunomodulants may be needed to enable CTL to become fully functional during ART.

HXB2 Location Env
Author Location gp140
Epitope
Immunogen Vaccine *Vector/Type:* protein, peptide in liposome *Strain:* B clade IIIB *HIV component:* gp140, gp160, oligomeric gp140 *Adjuvant:* CpG immunostimulatory sequence (ISS), liposome
Species (MHC) mouse
Donor MHC H-2d
Assay type cytokine production, proliferation, Chromium-release assay
Keywords Th1, Th2, adjuvant comparison, vaccine antigen design
References Rao *et al.* 2004

- Administration of ogp140 in liposomes containing lipid A (LA) induces high antibody titers which are increased by adding CpG ODN. Priming and boosting of BALB/c mice with ogp140+LA induces mixed Th1/Th2 immune response, while adding CpG ODN switches the immune response to a Th1 type. Mixing ogp140 with lipomoses containing lipid A yielded excellent proliferative and CTL specific responses; CpG did not affect CTL responses. The antigen did not need to be encapsulated in the liposome to induce strong responses with LA as an adjuvant.

HXB2 Location Env
Author Location
Epitope
Immunogen computer prediction
Species (MHC) (A*0201, B*3501)
Keywords inter-clade comparisons, computational epitope prediction
References Schönbach *et al.* 2002

- Computational methods (artificial neural networks, hidden Markov models, binding matrices based on HLA association rates) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.

HXB2 Location Env
Author Location
Epitope
Subtype A, B, C
Immunogen Vaccine *Vector/Type:* canarypox prime with gp120 boost, canarypox prime with gp160 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Nef, Pol
Species (MHC) human (A1, A2, A24, B62, A25, A26, A30, A31, B8, B17, B39, B51, B57, B60, B62, B70)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Ferrari *et al.* 2001

- Different HIV strains were used for different regions: gp41 LAI, Gag LAI, gp120 MN, gp120 SF2
- HLA-B62 responses dominated the responses against an Env vaccine in an individual (022JAV) who was HLA A2, A26, B35, B62. The strongest response was against the MN peptide 381-400; a response diminished by half was observed against vaccinia expressed clade A and clade C relative to clade B.
- Class I presentation of Env CTL responses in vaccinee 022A12K: A25 > B39, A1 and B8 were undetectable.
- Class I presentation of Env CTL responses in vaccinee 022A12N: B57 » A2 > A26 and B60.
- Class I presentation of Env CTL responses in vaccinee 034GP3: A31 > A24 > B62 > B51.
- Class I presentation of Env CTL responses in vaccinee 0348PP: B17 > B70, A1 and A30 were undetectable.

HXB2 Location Env
Author Location gp120 (303–327)
Epitope
Immunogen HIV-1 infection
Species (MHC) human (A2, A3, A11, B27)
Keywords inter-clade comparisons
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.
- For this cluster of epitopes spanning the tip of the V3 loop, they suggest including a sequence from each clade.

HXB2 Location Env
Author Location
Epitope
Subtype B
Immunogen Vaccine

Vector/Type: canarypox prime with gp120 boost, canarypox prime with gp160 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Nef, Pol
Species (MHC) human (A2, B8)
Keywords vaccine-induced epitopes
References Ferrari *et al.* 2001

- Different HIV strains were used for different regions: gp41 LAI, Gag LAI, gp120 MN, gp120 SF2
- No HLA-A*0201 or B8 responses were made against the Env vaccine in individuals carrying these alleles, despite these being common presenting molecules for CTL responses to natural infections.

HXB2 Location Env
Author Location Env
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*35)
Keywords rate of progression
References Jin *et al.* 2002

- Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501.
- Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env.
- The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.

HXB2 Location Env
Author Location gp41 (842–850 IIIB, BH8)
Epitope
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Pantaleo *et al.* 1997; Soudeyns & Pantaleo 1997

- Clonotype-specific PCR and analysis of *in vivo* HIV-specific CTL showed that in early infection HIV-specific CTL clones preferentially accumulate in blood rather than lymph nodes and that they accumulate prior to down-regulation of virus.

HXB2 Location Env
Author Location gp160 (MN)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade MN *HIV component:* gp120, gp160
Species (MHC) mouse (H-2^{d})
References Vinner *et al.* 1999

- Mammalian codon optimization renders gp160 expression Rev independent, increases gp160 expression levels, and DNA vaccination of BALB/c mice yields a higher antibody response with an earlier onset than wild type.
- Secreted gp120 gave higher antibody titers than membrane bound gp160.
- In contrast to antibodies, synthetic codon-optimized DNA did not alter the CTL response, wild type genes generated equally strong CTL responses.

HXB2 Location Env
Author Location (IIIB)
Epitope
Immunogen Vaccine
Vector/Type: peptide *HIV component:* V3 *Adjuvant:* Cholera toxin (CT), GM-CSF, IL-4
Species (MHC) mouse (H-2^{d})
References Kato *et al.* 2000

- A multicomponent peptide vaccine VC1 with cholera toxin adjuvant was given to mice.
- Immunization of BALB/c mice with VC1 and CT induced a strong CTL response which was enhanced by IL-12 expressing plasmids.
- Immunization with VC1 and CT resulted in HIV-1 specific IgA antibody responses, which were increased by the combination of IL-4 or GM-CSF expressing plasmids.

HXB2 Location Env
Author Location gp160 (IIIB)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* PLG
Species (MHC) mouse (H-2^{d})
References Kaneko *et al.* 2000

- A PLG-microparticle encapsulated DNA encoding gp160 was given to mice.
- Oral DNA vaccination of BALB/c mice induced mucosal and systemic gp160 glycoprotein-specific cellular and humoral immune responses, and mice vaccinated orally had higher resistance to HIV-env expressing vaccinia intrarectal challenge than mice vaccinated i.m.

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine
Vector/Type: DNA with CMV promotor with cationic liposome *HIV component:* gp160, Rev
Species (MHC) mouse (H-2^{d})
References Ishii *et al.* 1997

- pCMV160/Rev is a DNA vaccine candidate carrying gp160 and Rev linked to a cytomegalovirus (CMV promotor)

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine

Vector/Type: adeno-associated virus (AAV) *HIV component:* Env, Rev, Tat *Adjuvant:* IL-2
Species (MHC) mouse (H-2^d)
References Xin *et al.* 2001

- An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice.
- A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL.
- Boosting enhanced the humoral response, and IL2 enhanced T-cell immunity.

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine
Vector/Type: vaccinia, influenza *Strain:* B clade IIIB *HIV component:* Env, V3
Species (MHC) mouse (H-2^d)
References Gonzalo *et al.* 1999

- The use of two different live vectors for priming and boosting has a synergistic effect on the immune response against HIV-1– a 5-6 fold enhanced CTL response in Balb/c mice occurred when they were immunized with rec influenza virus (Flu-Env) expressing the V3 loop epitope from HIV-1 strain IIIB, and boosted with a vaccinia virus recombinant (VV-Env) expressing the complete HIV-1-IIIB env protein, comared to either immunogen alone.

HXB2 Location Env
Author Location Env (subtype B)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: rabies virus *Strain:* B clade 89.6, B clade NL43 *HIV component:* gp160
Species (MHC) mouse (H-2^d)
References McGettigan *et al.* 2001

- BALB/c were immunized with a replication competent recombinant rabies virus (RV) vaccine expressing HIV-1 gp160.
- A single vaccination induced induced strong and long-lasting (4.5 months) gp160-specific CTL cytotoxic responses.
- Although the greatest specific lysis was achieved when the vaccine strain was also used as the *in vitro* the target strain to assess the response, there was extensive CTL cross-reactivity against other B clade HIV-1 envelope proteins, implying CTL recognition of multiple epitopes within the HIV-1 envelope protein.

HXB2 Location Env
Author Location gp120 (V3)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA, polyepitope *Strain:* B clade BRVA, B clade IIIB, B clade JY1, B clade LR150, B clade MN, B clade RF *HIV component:* V3
Species (MHC) mouse (H-2^d)
Assay type CD8 T-cell Elispot - IFNγ
References Vázquez-Blomquist *et al.* 2003

- Priming mice with recombinant MVA and boosting with fowlpox was shown to increase the number of specific IFN-gamma secreting cells relative to reversing the order (fowlpox prime, MVA boost) or priming with a Semliki Forest Virus DNA vector and boosting with recombinant MVA or fowlpox. The authors speculate why the order might be important. Fowlpox has more proteins, so there may be more CTL epitope competition; alternatively pox viruses may modulate the immune response through chemokine homologs.
- The antigen tested was a V3 loop polyepitope vaccine combining multiple V3 loop variants given by an intraperitoneal route to BALB/c mice.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* gp120 *Adjuvant:* Cholera toxin (CT)
Species (MHC) mouse (H-2D^d)
Assay type T-cell Elispot, Chromium-release assay
References Bagley *et al.* 2003

- BALBc mice were immunized intramuscularly with single plasmids encoding gp120, or cholera toxin catalytic domain (CTA1) and gp120, or with a dicistronic DNA vaccine expressing both CTA1 and gp120. Vaccination including CTA elicited stronger and longer lasting Ab responses and T-cell responses to gp120.

HXB2 Location Env
Author Location Env (SIV)
Epitope
Immunogen SIV infection
Species (MHC) macaque (Mamu-A*11, -B*03, -B*04, -B*17)
References Dzuris *et al.* 2000

- Cell binding assays for Mamu molecules were employed to describe the peptide binding motifs for Mamu-A*11, -B*03, -B*03, -B*04, and -B*17 CTL epitopes – a similarity for Mamu-A*11 and -B*03 and human HLA-B*44 and -B*27, respectively, was observed – all epitopes studied were SIV epitopes, so not specifically listed here.

II-B-21 Nef CTL, CD8+, epitopes

HXB2 Location Nef (1–16)
Author Location Nef (1–16)
Epitope MGGKWSKSSIVGWPAV
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.

- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Nef (13–20)
Author Location Nef (13–20 LAI)
Epitope WPTVRERM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Keywords optimal epitope
References Frahm *et al.* 2004; Goulder *et al.* 1997g

- C. Brander notes this is a B*0801 epitope.

HXB2 Location Nef (13–20)
Author Location Nef (HXB2)
Epitope WPTVRERM
Subtype B
Immunogen HIV-1 infection
Species (MHC) (B*0801)
Keywords class I down-regulation by Nef
References Peng & Robert-Guroff 2001

- Deletion of the 19 N-terminal amino acids from Nef including the myristolation signal eliminates Nef-induced down-regulation of MHC class I and CD4 molecules. Such a construct has the potential to serve as a more potent immunogen. The known T-cell epitopes that that would be disputed by this deletion are minimal, including the HLA-B8 CTL epitope WPTVRERM.

HXB2 Location Nef (13–20)
Author Location (C consensus)
Epitope WPAIRERM
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Nef (13–20)
Author Location Nef (13–20 LAI)
Epitope WPTVRERM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Goulder *et al.* 1997g

- Unusual epitope for HLA-B8, but compatible with crystal structure predictions.

HXB2 Location Nef (13–20)
Author Location Nef (13–20)
Epitope WPTVRERM
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope as well as seven others.

HXB2 Location Nef (13–20)
Author Location Nef (13–20 SF2)
Epitope WPTVRERM
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/3 group 2, and 1/2 group 3.

HXB2 Location Nef (13–20)
Author Location Nef (13–20)
Epitope WPTVRERM
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Day *et al.* 2001

- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.

HXB2 Location Nef (19–27)
Author Location Nef (19–27)
Epitope RMRRAEPAA
Immunogen HIV-1 infection
Species (MHC) human (B*1501)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (19–27)

Author Location Nef (19–27)
Epitope RMRRAEPAA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B62)
Donor MHC A*0201, A29, B58, B62, Cw*0301, Cw*1601
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location Nef (37–45)
Author Location Nef (37–45)
Epitope LEKHGAITS
Immunogen HIV-1 infection
Species (MHC) human (B*4001)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (37–45)
Author Location Nef (37–45)
Epitope LEKHGAITS
Immunogen
Species (MHC) human (B*50)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (42–50)
Author Location Nef (44–52 HXB3)
Epitope ALTSSNTAA
Immunogen Vaccine
Vector/Type: DNA, peptide *Strain:* B clade HXB3 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (A*0201)
Keywords binding affinity, computational epitope prediction
References Sandberg *et al.* 2000

- Ten Nef 9-mer peptides were predicted to have a strong binding affinity with HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly.
- A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with either nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by gene gun.
- ALTSSNTAA was also tested by subcutaneous injection of Nef peptides in Freund's adjuvant.
- ALTSSNTAA bound weakly to HLA-A2, but it had the strongest CTL response among the three elicited by the DNA vaccine and a strong response to the peptide vaccination.

HXB2 Location Nef (42–50)
Author Location Nef (42–50)
Epitope ALTSSNTAA
Epitope name Nef42-50
Immunogen HIV-1 infection
Species (MHC) human, humanized mouse (A2)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords responses in children, immunodominance, characterizing CD8+ T cell responses
References Chandwani *et al.* 2004

- Responses to five HLA-A2 presented epitopes in Nef were characterized in a population of 19 HIV infected adults and 21 children. The CD8 T-cell response to Nef was stronger and broader in adults than children, averaging 652 and 87 SFCs/10^6 PBMC, and 2.6 and 0.9 recognized epitopes per person, respectively.
- This is one of three novel Nef epitopes previously identified in HLA-A2 transgenic mice, shown to induce CD8 T-cell response in humans. It was not the immunodominant response.

HXB2 Location Nef (48–56)
Author Location Nef (58–66 JRFL)
Epitope TAATNADCA
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade JRFL
Species (MHC) mouse (H-2^b)
References Liang *et al.* 2002

- BALB/c, C3H/HeN and C57BL/6 mice were given intramuscular immunization with Nef DNA constructs – C57BL/6 responded to this epitope.
- The Nef mutant that lacked the myristylation site (G–>A) at position 2, and the dileucine motif (L –> A at positions 174 and 175) was impaired in terms of its ability to elicit induction of Nef-specific CD4+ and CD8+ T-cell responses. The myristylation site is critical for Nef membrane localization and function, and the di-leucine motif for the down-regulation of surface CD4 molecules, and the mutation of these regions could yield a safer vaccine.
- N-terminal addition of human tissue plasminogen activator (TPA) to Nef, enhanced CD8+ T-cell responses and could compensate for the G2A, L174A, L175A mutations – this enhanced immunogenicity correlated with enhanced levels of protein expression in transfected cells.

HXB2 Location Nef (50–58)
Author Location Nef (50–)
Epitope ATNADCAWL
Epitope name Nef50
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* Nef *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a low A2-binder that did not induce CTL or CD8+ T-cell IFN gamma responses in mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.

HXB2 Location Nef (62–81)
Author Location Nef (61–80)
Epitope EEEEVGFPVTPQVPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location Nef (62–81)
Author Location Nef (61–80 SF2)
Epitope EEEEVGFPVTPQVPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- Two of these 12 had CTL response to this peptide.
- The responding subjects were HLA-A11, A24, B8, B35, and HLA not determined.

HXB2 Location Nef (62–81)
Author Location Nef (61–80 SF2)
Epitope EEEEVGFVTPQVPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location Nef (62–81)
Author Location Nef (SF2)
Epitope EEEEVGFPVTPQVPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2001a

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- Nef peptides PQVPLRRMTYKAAVDLSHFL, KAAVDLSHFLKEKGGLEGLI and EEEEVGFPVTPQVPLRPMTY were recognized and the first two share KAAVDLSHFL (a Cw8 epitope), the first and last share PQVPLRPMTY.

HXB2 Location Nef (64–74)
Author Location Nef (C consensus)
Epitope GEVGFPVRPQV
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B45)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords escape, reversion, viral fitness
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- People who carried B45 tended to carry a variant of this epitope, while people who did not almost always carried the consensus form.
- B*4501 was one of the HLA types associated with having a high viral load.

HXB2 Location Nef (66–80)
Author Location Nef (66–80 BRU)
Epitope VGFPVTPQVPLRMT
Immunogen HIV-1 infection
Species (MHC) human (A1, B8)
References Hadida *et al.* 1992

- HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.

HXB2 Location Nef (66–80)
Author Location Nef (64–78)
Epitope VGFPVTPQVPLRMT
Immunogen HIV-1 infection
Species (MHC) human (A1, B8)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Nef (66–97)
Author Location Nef (66–97 LAI)
Epitope VGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide

Species (MHC) human
References Gahery-Segard *et al.* 2000
- Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 5/10 reacted to this Nef peptide.
- 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual.
- 5/12 tested had an IgG response to this peptide.

HXB2 Location Nef (67–81)
Author Location Nef (67–81)
Epitope GFPVRPQVPLRPMTY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002
- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Nef (68–76)
Author Location Nef (68–76)
Epitope FPVTPQVPL
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (68–76)
Author Location Nef (72–80 SF2)
Epitope FPVRPQVPL
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 1997
- A CTL clone responsive to this epitope was obtained.
- 3/7 B35-positive individuals had a CTL response to this epitope.
- An R to T substitution at position 4 abrogates specific lysis, but not binding to B*3501.

HXB2 Location Nef (68–76)
Author Location Nef (72–80)
Epitope FPVRPQVPL
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 2000a
- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A.
- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals.
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm.
- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

HXB2 Location Nef (68–76)
Author Location Nef (72–80 SF2)
Epitope FPVRPQVPL
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Shiga *et al.* 1996
- Binds HLA-B*3501.

HXB2 Location Nef (68–76)
Author Location (SF2)
Epitope FPVRPQVPL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords rate of progression
References Kawana *et al.* 1999
- HLA B35 is associated with rapid disease progression.
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals.
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation.

HXB2 Location Nef (68–76)
Author Location Nef (66–74)
Epitope FPVRPQVPL
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Ferrari *et al.* 2000
- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Nef (68–76)
Author Location Nef (68–76 BRU)
Epitope FPVTPQVPL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001
- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.

- FPVTPQVPL was recognized in 1/13 (8%) of individuals with HLA B7, and 1/12 (8%) of individuals with HLA B35. It was a high affinity HLA binder.

HXB2 Location Nef (68–76)
Author Location Nef (68–76)
Epitope FPVTPQVPL
Immunogen in vitro stimulation or selection
Species (MHC) human (B7)
Keywords binding affinity, dendritic cells, Th1
References Wilson *et al.* 1999b

- Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors.
- Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within.
- B7 and A2 Nef epitopes were studied – FPVTPQVPL has a high affinity for B7.

HXB2 Location Nef (68–76)
Author Location Nef (68–76)
Epitope FPVTPQVPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location Nef (68–76)
Author Location Nef (68–76 BRU)
Epitope FPVTPQVPL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- FPVTPQVPL was recognized in 1/13 (8%) of individuals with HLA B7, and 1/12 of individuals with HLA B35. It was a high affinity HLA binder.

HXB2 Location Nef (68–76)
Author Location Nef (68–76)
Epitope FPVTPQVPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. Also, none of 4 individuals had detectable responses to this epitope after STI.

HXB2 Location Nef (68–76)
Author Location Nef (68–76)
Epitope FPVTPQVPL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B7 supertype)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the most frequently recognized of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location Nef (68–77)
Author Location Nef (68–77 LAI)
Epitope FPVTPQVPLR
Subtype B
Immunogen HIV-1 infection

Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0702 epitope.

HXB2 Location Nef (68–77)
Author Location Nef (68–77 LAI)
Epitope FPVTPQVPLR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Haas *et al.* 1996

- There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection.

HXB2 Location Nef (68–77)
Author Location Nef (subtype B)
Epitope FPVTPQVPLR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HIV exposed persistently seronegative (HEPS), escape
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- FPVTPQVPLR was recognized in 1 of the 6 women (ML1203), and the response was present in the last available sample prior to seroconversion, 7 months.
- 20/20 sequences of the infecting strain had no substitutions in this epitope, all were FPVTPQVPLR, so there was no evidence for escape.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized in 1/22 HEPS sex worker controls, ML851.

HXB2 Location Nef (68–77)
Author Location Nef (66–75)
Epitope FPVRPQVPLR
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Nef (68–77)
Author Location Nef (68–77 SF2)
Epitope FPVTPQVPLR
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3.

HXB2 Location Nef (68–77)
Author Location Nef (68–77)
Epitope FPVTPQVPLR
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B7)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPG(V/I)RYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.

HXB2 Location Nef (68–77)
Author Location Nef (68–77)
Epitope FPVTPQVPLR
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location Nef (68–77)
Author Location Nef (68–76)
Epitope FPVTPQVPLR
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. Also, none of 4 individuals had detectable responses to this epitope after STI.

HXB2 Location Nef (68–77)
Author Location Nef (66–75)
Epitope FPVTPQVPLR
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 7 patients recognized this epitope.

HXB2 Location Nef (68–81)
Author Location Nef (82–95 HXB2)
Epitope FPVTPQVPLRMTY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Guimaráes *et al.* 2002

- Nef sequences were obtained from Brazilians to study epitope diversity in this geographic region—the HXB2 sequence is FPVTPQVPLRMTY, but fpvRpqvplrmty was observed in most Brazilian sequences regardless of the subtype (A, C, D and F).

HXB2 Location Nef (68–84)
Author Location Nef
Epitope FPVRPQVPLRPMTYKGA
Immunogen
Species (MHC) human
Keywords inter-clade comparisons
References Jubier-Maurin *et al.* 1999

- 41 new HIV-1 strains describing envelope subtypes of HIV-1 A-H were genetically characterized in the nef region – 34 subtypes were classified in the same subtype in nef and env and 7 of the 41 strains were recombinants.
- This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes.

HXB2 Location Nef (70–84)
Author Location Nef (70–84 HXB2)
Epitope VTPQVPLRPMTYKAA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 34% of the study subjects, and it was the second most frequently recognized peptide.

HXB2 Location Nef (71–79)
Author Location Nef (71–79 LAI)
Epitope TPQVPLRPM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords optimal epitope

References Frahm *et al.* 2004

- C. Brander notes this is a B*0702 epitope.

HXB2 Location Nef (71–79)
Author Location Nef (71–79 BRU)
Epitope TPQVPLRPM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- TPQVPLRPM was recognized in 1/10 (10%) of individuals with HLA B7, and 1/10 (10%) of individuals with HLA B35. It was a moderate affinity HLA binder.

HXB2 Location Nef (71–79)
Author Location Nef (71–79 SF2)
Epitope TPQVPLRPM
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3.

HXB2 Location Nef (71–79)
Author Location Nef (71–79)
Epitope TPQVPLRPM
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location Nef (71–79)
Author Location Nef (71–79 BRU)
Epitope TPQVPLRPM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- TPQVPLRPM was recognized in 1/10 (10%) of individuals with HLA B7, and 1/10 (10%) individuals with HLA B35. It was a moderate affinity HLA binder.

HXB2 Location Nef (71–79)
Author Location Nef (71–79)
Epitope TPQVPLRPM
Epitope name B7-TM9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.

- 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.

HXB2 Location Nef (71–79)
Author Location Nef
Epitope TPQVPLRPM
Epitope name B7-TM9(Nef)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A32, A?, B7, B14; A24, A?, B7, B27
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT). Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).

HXB2 Location Nef (71–79)
Author Location Nef (71–79)
Epitope TPQVPLRPM
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B7 supertype)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the most frequently recognized of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location Nef (71–79)
Author Location Nef (C consensus)
Epitope RPQVPLRPM
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B7, B81, B*4201, B*0702, B*8101)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords escape, cross-presentation by different HLA
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- People who carried either B07 or B81 tended to carry a variant of this epitope, while people who did not almost always carried the consensus form.
- B*4201 may also present this epitope, as the allele is enriched in people who react with the peptide that contains the epitope, and it is known from the database to be also presented by B*4201.

HXB2 Location Nef (71–81)
Author Location Nef (75–85 SF2)
Epitope RPQVPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 1997

- A CTL clone responsive to this epitope was obtained.
- 4/7 B35-positive individuals had a strong CTL response to this epitope.
- An R to T substitution at position 1 abrogates specific lysis, but not binding to B*3501.
- An R to H substitution at position 7 did not alter reactivity.

HXB2 Location Nef (71–81)
Author Location Nef (75–85)
Epitope RPQVPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
References Tomiyama *et al.* 2000a

- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A.
- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals.
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm.

- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

HXB2 Location Nef (71–81)
Author Location Nef (75–85 SF2)
Epitope RPQVPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Shiga *et al.* 1996

- Binds HLA-B*3501.

HXB2 Location Nef (71–81)
Author Location (SF2)
Epitope RPQVPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, rate of progression, escape
References Kawana *et al.* 1999

- HLA B35 is associated with rapid disease progression.
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals.
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation.
- rpqvplrpmtF was found in 9/10 of the B35+ individuals, none of the B35- individuals—the Y–>F substituted peptide had a similar binding affinity with B35 and was recognized by a CTL clone equally with wildtype.

HXB2 Location Nef (71–81)
Author Location Nef (69–79)
Epitope RPQVPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Nef (71–81)
Author Location Nef (71–81 BRU)
Epitope TPQVPLRPMTY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- TPQVPLRPMTY was recognized in 9/12 (75%) of individuals with HLA B7, and 5/10 (50%) of individuals with HLA B35. It was a moderate affinity HLA binder, and the C-term Y readily cleaved *in vitro*.

HXB2 Location Nef (71–81)
Author Location Nef
Epitope RPQVPLRPMTY
Subtype A, B, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human, macaque (B51)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location Nef (71–81)
Author Location Nef (71–81 BRU)
Epitope TPQVPLRPMTY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- TPQVPLRPMTY was recognized in 9/12 (75%) of individuals with HLA B7, and 5/10 (50%) of individuals with HLA B35. It was a moderate affinity HLA binder, and the C-term Y readily cleaved *in vitro*.

HXB2 Location Nef (71–81)
Author Location Nef (71–81)
Epitope TPQVPLRPMTY
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B7 supertype)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.
- A response was induced in one patient after immuniaation with lipopeptides alone (no adjuvant) after the third (W44) boost. A rPQVPLRPMTY variant was also recognized.

HXB2 Location Nef (72–81)
Author Location Nef (72–82)
Epitope PQVPLRPMTY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35, B51)
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- Three of nine patients responded to this peptide with GzB producing and IFN-gamma producing cells, and one additional with IFN-gamma producing cells.

HXB2 Location Nef (72–86)
Author Location Nef (72–86)
Epitope PQVPLRPMTYKGAFD
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Nef (72–91)
Author Location Nef (71–90 SF2)
Epitope PQVPLRMTYKAAVDLSHFL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- Three of these 11 had CTL response to this peptide.
- The responding subjects were HLA-A3, A32, B51, B62; HLA-A11, A24, B8, B53.

HXB2 Location Nef (72–91)
Author Location Nef (71–90 SF2)
Epitope PQVPLRPMTYKAAVDLSHFL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location Nef (72–91)
Author Location Nef (SF2)
Epitope PQVPLRRMTYKAAVDLSHFL
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2001a

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- Nef peptides PQVPLRRMTYKAAVDLSHFL, KAAVDLSH-FLKEKGGLEGLI and EEEEVGFPVTPQVPLRPMTY were recognized and the first two share KAAVDLSHFL (a Cw8 epitope), the first and last share PQVPLRPMTY.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human
References Garcia *et al.* 1997

- The anti-Nef CTL line P1 specific for this epitope is able to kill target cells via two mechanisms.
- First: Ca^{2+}-dependent, perforin-dependent Nef-specific lysis.
- Second: Ca^{2+}-independent, CD95-dependent apoptosis that could also kill non-specific targets.
- Findings indicate that the two mechanisms are not mutually exclusive in human CTL, as they are in mice.
- CTL mediated CD95-dependent apoptosis may play a role in pathogenesis.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 NL43)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)

References Koenig *et al.* 1990

- 81 Tyr is critical for binding to A3.1.
- C. Brander notes that this is an A*0301 epitope in the 1999 database.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A*0301)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope QVPLRPMTYK
Subtype B
Immunogen
Species (MHC) human (A*0301)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0301 epitope.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0301)
Keywords epitope processing, dendritic cells
References Andrieu *et al.* 2003

- This study demonstrates that lipopeptides carrying epitopes can be taken up by human dendritic cells, processed using different pathways, and recognized by epitope-specific CD8+ T-cells originally derived from HIV+ individuals. The RT ILKEPVHGV peptide was embedded in a longer peptide fragment in the lipopeptide, and was internalized by endocytosis and processed in the cytosol by proteasomal cleavage by following an endosome-to-cytosol pathway for processing and presentation. Administration of epoxomycin, a proteasome inhibitor, completely abrogated epitope presentation to a CD8+ T-cell line, while monensin, an inhibitor of acid-dependent endosomal enzyme activity did not.
- In contrast to the RT epitope, dendritic cell presentation of the Nef epitope QVPLRPMTYK embedded in a longer peptide in a lipopeptide was not inhibited by epoxomycin, but was inhibited by monensin, indicative of endocytolitic epitope processing.

HXB2 Location Nef (73–82)
Author Location Nef
Epitope QVPLRPMTYK
Subtype A, B, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade
HIV component: p17 Gag, p24 Gag
Species (MHC) human, macaque (A*0301, A11)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Subtype B, CRF01_AE
Immunogen
Species (MHC) (A*1101)
Country Thailand.
Keywords HIV exposed persistently seronegative (HEPS), immunodominance, structure
References Li & Bouvier 2004

- HLA-A*1101 has been associated with resistance to acquisition of HIV-1 infection in female sex-workers in Thailand. Its crystal structure has been determined in association with two immunodominant A*1101 HIV-1 CTL epitopes. Its anchor residues are confirmed as P2(Ile/Val) and C-term (Lys). The backbone conformation of the peptides is defined as two bulges

separated by a secondary anchor residue (P6 Ser or Met) that may offer various advantages in the selection and presentation of CTL epitopes by HLA-A*1101.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Le Borgne *et al.* 2000

- Soluble factors in supernatant from both an HIV-specific cloned CTL line and an EBV (Epstein-Barr-virus) CTL line inhibit viral replication, but do not block viral entry in CD4+ T lymphocytes, by a noncytotoxic mechanism.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope QVPLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Robertson *et al.* 1993

- Development of a retroviral vector (pNeoNef) to generate autologous CTL targets.
- Hunziker *et al.* [1998] suggests that HLA-A2 does not in fact present this epitope.
- The initial assignment of HLA-A2 presentation for this epitope was based on a serological HLA typing. Subsequently, the authors revisited the issue with genetic HLA typing and found that HLA-A11 was the correct presenting molecule (Dr. Florence Buseyne, pers. comm., 2000)

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope QVPLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords review, escape
References Couillin *et al.* 1994; Goulder *et al.* 1997a

- Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope QVPLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Couillin *et al.* 1995

- Mutations found in this epitope in HLA-A11 positive and negative donors were characterized.

HXB2 Location Nef (73–82)
Author Location (LAI)
Epitope QVPLRPMTYK
Subtype B
Immunogen
Species (MHC) (A11)
Keywords optimal epitope
References Buseyne 1999; Frahm *et al.* 2004

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Epitope name QVP
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- One of the 2/8 HLA-A11 study subjects recognized this CTL epitope.
- Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Appay *et al.* 2000

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

HXB2 Location Nef (73–82)
Author Location Nef (71–80 93TH253 subtype CRF01)
Epitope QVPLRPMTYK
Epitope name N73-82
Subtype CRF01_AE
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was weakly reactive in HEPS study subjects 265 who was HLA A2/A11 and 128 who was HLA A11/A33, and after a second *in vitro* stimulation, in study subject 256 who was HLA A11/33, making it the most reactive epitope tested in HLA-A11 HEPS women, with 3/4 responding.
- This epitope was strongly reactive in HIV+ study subject 053 who carried HLA-A11.

HXB2 Location Nef (73–82)
Author Location Nef (71–80 93TH253 subtype CRF01)
Epitope QVPLRPMTYK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined.
- 4/8 tested FSWs recognized this epitope.
- An HLA-A11 tetramer was made for this epitope, which was recognized by two subjects – only one subject had an expanded tetramer staining T-cell population after *in vitro* stimulation.
- This epitope was highly conserved in other subtypes, and exact matches were common.

HXB2 Location Nef (73–82)
Author Location Nef
Epitope QVPLRPMTYK
Epitope name QVP
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location Nef (73–82)
Author Location Nef
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A11)
Donor MHC A2, A11, B8, B60, Bw6
Keywords HAART, ART
References Appay *et al.* 2002

- Four HIV patients with prolonged clinically successful antiviral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized this epitope, one using HLA-A3, one using HLA-A11.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11, A*0301)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- None of three patients responded to this peptide with GzB producing cells, while all three responded with IFN-gamma producing cells.

HXB2 Location Nef (73–82)
Author Location Nef (73–81)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A2, A3, A11, B35)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope QVPLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords epitope processing, escape
References Chassin *et al.* 1999

- Mutations in Nef that flank this epitope, Thr71Lys and Ala83Gly, may account for an observed loss of CTL reactivity, with escape due to the introduction of proteasome processing defects.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords inter-clade comparisons
References Durali *et al.* 1998

- Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia.
- Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested.
- Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag.
- Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef.
- Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env.
- One of the patients was shown to react to this epitope: QVPLRPMTYK.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope QVPLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords review, escape
References Goulder *et al.* 1997e; Goulder *et al.* 1997a

- HLA-identical siblings, twin hemophiliac brothers, were both infected with the same batch of factor VIII.
- Both had a response to this epitope. One had a response to this epitope, the other did not.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Lubaki *et al.* 1997

- Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response.
- A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response.
- An A3+ subject had a strong response to this epitope, with 10/11 CTL clones being specific for this epitope, isolated at two time points, 1 year apart.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Epitope name N1
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords HAART, ART, escape
References Samri *et al.* 2000

- The epitope was recognized by patients 252#0 and 252#4 in a study of the effects of therapy escape mutations on CTL recognition.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 SF2)
Epitope QVPLRRMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 3/7 group 1, 1/4 group 2, and 1/2 group 3.

HXB2 Location Nef (73–82)
Author Location Nef (SF2)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.

HXB2 Location Nef (73–82)
Author Location
Epitope QVPLRPMTYK
Epitope name Nef-QK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)

References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A03, 9/20 (45%) recognized this epitope.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Epitope name A3-QK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 3/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 5/7 individuals had detectable responses to this epitope after STI.

HXB2 Location Nef (73–82)
Author Location Nef
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B44, B64, Bw4, Bw6
Keywords HAART, ART
References Appay *et al.* 2002

- Four HIV patients with prolonged clinically successful antiviral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized this epitope, one using HLA-A3, one using HLA-A11.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A1, A3, B7, B14, Cw*0702, Cw*0802
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 17 potential epitopes from this individual, defined based on previously identified epitopes presented by appropriate HLA molecules. Full length genome sequence did not reveal changes in time in any of these epitopes over a four year period. Peptide pools initially revealed very little response to these eptiopes, but this increased over time.

HXB2 Location Nef (73–82)
Author Location Nef
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- 3/5 HLA A3+ infection-resistant men, compared to 1/3 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location Nef (73–82)
Author Location Nef (71–80)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong T-helper cell responses. Only patients starting with moderately high viral load (VL) were able to reduce the VL set point. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up.
- 9/14 patients recognized this epitope, it was the most recognized of six A*03 epitopes.

HXB2 Location Nef (73–82)
Author Location (B consensus)
Epitope QVPLRPMTYK
Epitope name QK10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A03, B14, B60, Cw3, Cw7; A01, A03, B08, B14, Cw7, Cw8
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 2/9 individuals recognized this epitope, presented by HLA-A3.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope QVPLRPMTYK
Epitope name N1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords HAART, ART, supertype
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location Nef (73–82)
Author Location Nef (94–103)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).

HXB2 Location Nef (73–82)
Author Location Nef (73–82 BRU)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3, A11, B35)
References Culmann *et al.* 1991

- Nef CTL clones from HIV+ donors.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope QVPLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3.1)
Keywords rate of progression, escape
References Koenig *et al.* 1995

- Alanine substitutions L76A, R77A, M79A, T80A significantly decreased immunogenicity of peptide.

- Nef CTL clones (4N225) were infused into an HIV-1 infected volunteer to evaluate effects of infusion on viral load/patient health.
- Infusion led to outburst of escape variants which resulted in higher viral load/accelerated disease progression.

HXB2 Location Nef (73–82)
Author Location Nef (73–82)
Epitope QVPLRPMTYK
Immunogen HIV-1 infection
Species (MHC) human (A3.1)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was A3, and responded to QVPLRPMTYK as well as two other A3.1 epitopes.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope QVPLRPMTYK
Subtype B
Immunogen
Species (MHC) human (B27)
References Culmann 1998

- Optimal epitope mapped by peptide titration.

HXB2 Location Nef (73–82)
Author Location Nef (73–82 LAI)
Epitope SVPLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35, Cw4)
References Buseyne *et al.* 1993a

- Vertical transmission of HIV ranges from 13% to 39%.
- Primary assays showed that cytotoxic activity against at least one HIV protein was detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study.

HXB2 Location Nef (73–82)
Author Location
Epitope QVPLRPMTYK
Epitope name QK10
Immunogen HIV-1 infection
Species (MHC) human (B8)
Country United States.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Tetramer binding
Keywords immunodominance, acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Lichterfeld *et al.* 2004a

- HIV-1 specific CD8+ T-cells in acute and long-term nonprogressive HIV-1 infection show strong ex-vivo proliferative capacities which are rapidly lost in chronic HIV-1 infection. The loss of CD8+ T-cell function is closely linked with the loss of HIV-1 specific, IL2 secreting CD4+ T-cells. The function can be rescued in vitro and in vivo by restoring the specific CD4+ T-cell help.
- Full CD8+ T-cell responses to this epitope were dependent on co-stimulation with a CD4+ T cell dependent epitope from T-cells harvested during acute infection. The CD8+ T-cell response to this epitope was immunodominant in one study individual.

HXB2 Location Nef (73–83)
Author Location Nef (73–82 BRU)
Epitope QVPLRPMTYKA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- QVPLRPMTYKA was recognized in 9/15 (60%) of individuals with HLA A3. It was a high affinity HLA-A3 binder.

HXB2 Location Nef (74–81)
Author Location Nef (74–82)
Epitope VPLRPMTY
Immunogen
Species (MHC) human (A3)
References Carreno *et al.* 1992

- Included in HLA-A3 binding peptide competition study.

HXB2 Location Nef (74–81)
Author Location Nef (73–82 LAI)
Epitope VPLRPMTY
Subtype B
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human (B*3501)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*3501 epitope.

HXB2 Location Nef (74–81)
Author Location Nef (75–82)
Epitope VPLRPMTY
Immunogen Peptide-HLA interaction
Species (MHC) human (B*3501)
References Smith *et al.* 1996

- Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex.

HXB2 Location Nef (74–81)
Author Location Nef
Epitope VPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human (B*3501)
Keywords dendritic cells
References Ostrowski *et al.* 2000

- The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*
- Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients.
- Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes.
- The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)

HXB2 Location Nef (74–81)
Author Location Nef (subtype B)
Epitope VPLRPMTY
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B35)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location Nef (74–81)
Author Location Nef
Epitope VPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location Nef (74–81)
Author Location Nef (73–82 LAI)
Epitope VPLRPMTY
Subtype B
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human (B35)
Keywords review
References Culmann *et al.* 1991; McMichael & Walker 1994

- Review of HIV CTL epitopes – defined by B35 motif found within a larger peptide.

HXB2 Location Nef (74–81)
Author Location Nef (73–82 LAI)
Epitope VPLRPMTY
Subtype B
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human (B35)
References Rowland-Jones *et al.* 1995

- VPLRPMTY also recognized by CTL from HIV-2 seropositives; epitope is conserved.

HXB2 Location Nef (74–81)
Author Location Nef
Epitope VPLRPMTY
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B35)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A and D subtype consensus are identical to the B clade epitope.

HXB2 Location Nef (74–81)
Author Location Nef (75–82)
Epitope VPLRPMTY
Immunogen in vitro stimulation or selection
Species (MHC) human (B35)
References Lalvani *et al.* 1997

- A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers.

- This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors.

HXB2 Location Nef (74–81)
Author Location Nef (subtype B)
Epitope VPLRPMTY
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B35)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among A, B, and D clade viruses.

HXB2 Location Nef (74–81)
Author Location Nef
Epitope VPLRPMTY
Immunogen
Species (MHC) human (B35)
References Rowland-Jones *et al.* 1999

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive,
- HIV-2 version of this epitope is conserved: VPLRPMTY, and CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also Rowland-Jones *et al.* [1995]

HXB2 Location Nef (74–81)
Author Location Nef (74–81)
Epitope VPLRPMTY
Epitope name VPL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- One of two HLA B35+ among the eight study subjects recognized this epitope.
- Patient SC15 (HLA A1/68, B8/35, Bw4/6, Cw4/0704) was given acute and sustained therapy and recognized epitopes PPIPVGDIY and VPLRPMTY during 331 days of HAART treatment.

HXB2 Location Nef (74–81)
Author Location Nef (75–82)
Epitope VPLRPMTY
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B35)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion.

HXB2 Location Nef (74–81)
Author Location
Epitope VPLRPMTY
Epitope name Nef-VY8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B35, 12/22 (55%) recognized this epitope.
- Among HIV+ individuals who carried HLA B*5301, 0/11 (0%) recognized this epitope.

HXB2 Location Nef (74–81)
Author Location Nef (74–81 BRU)
Epitope VPLRPMTY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- VPLRPMTY was recognized in 5/16 (31%) of individuals with HLA B35, and it was a moderate affinity HLA binder. Cleavage at the C-term Y was frequent *in vitro*.

HXB2 Location Nef (74–81)
Author Location
Epitope VPLRPMTY
Subtype A, B, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade
HIV component: p17 Gag, p24 Gag
Species (MHC) human, macaque (B35)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location Nef (74–81)
Author Location Nef (74–81)
Epitope VPLRPMTY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Donor MHC A1, A3, B8, B35
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early treatment
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. SubjectBroadcast message from root Thu May 27 21:34:36 2004...n of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma vBattery Low Notification from APM BIOS (8% 0:12)or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location Nef (74–81)
Author Location Nef (72–79)
Epitope VPLRPMTY
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 9 patients recognized this epitope.

HXB2 Location Nef (74–81)
Author Location Nef (C consensus)
Epitope VPLRPMTY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B35)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords escape
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- People who carried B35 carried a variant of this epitope, while people who did not almost always carried the consensus form.

HXB2 Location Nef (74–81)
Author Location Nef (72–79)
Epitope VPLRPMTY
Epitope name VPL
Immunogen HIV-1 infection
Species (MHC) human (B35)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, immunodominance, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- VPL epitope was one of six that were largely or completely replaced by escape variants, with the two escape forms coming up between days 172 and 635, vplrpmSy and vplrmptF.

HXB2 Location Nef (74–82)
Author Location Nef (73–82)
Epitope VPLRPMTYK
Immunogen Peptide-HLA interaction
Species (MHC) human (A11)
References Zhang *et al.* 1993
- Exploration of A11 binding motif.

HXB2 Location Nef (75–82)
Author Location Nef (75–82 LAI)
Epitope PLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords review
References McMichael & Walker 1994
- Review of HIV CTL epitopes.
- C. Brander notes that this is an A*1101 epitope in the 1999 database.

HXB2 Location Nef (75–82)
Author Location Nef (75–82 LAI)
Epitope PLRPMTYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is an A*1101 epitope.

HXB2 Location Nef (77–85)
Author Location Nef (79–85)
Epitope RPMTYKAAV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A3, A33, B14, B35, Cw*0401, Cw*0802
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early treatment
References Cao *et al.* 2003
- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location Nef (77–85)
Author Location Nef (77–85 LAI)
Epitope RPMTYKAAL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords escape
References Bauer *et al.* 1997
- Structural constraints on the Nef protein may prevent escape.
- Noted in Brander 1999, this database, to be B*0702.

HXB2 Location Nef (77–85)
Author Location Nef (77–85 LAI)
Epitope RPMTYKAAL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*0702 epitope.

HXB2 Location Nef (77–85)
Author Location Nef (75–83 IIIB)
Epitope RPMTYKAAL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords binding affinity, TCR usage
References Oxenius *et al.* 2001b
- Study of tetramer staining of B7 around RPMTYKAAL gave quantitative results that were very different than functional measurements based on an ELISPOT assay.
- Autologous clones were checked and 39/40 clones from two time points had the variant sequence RPMTYKGAL – tetramers based on RPMTYKGAL gave a more intense and uniform staining and bound with higher affinity to the RPMTYKGAL Vβ14 TCR.

HXB2 Location Nef (77–85)
Author Location Nef (77–85 SF2)
Epitope RPMTYKAAL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 1/4 group 1, 0/3 group 2, and 1/1 group 3.

HXB2 Location Nef (77–85)
Author Location Nef (77–85)
Epitope RPMTYKAAL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location Nef (77–85)
Author Location Nef (77–85)
Epitope RPMTYKAAV
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location Nef (77–85)
Author Location Nef (77–85 BRU)
Epitope RPMTYKAAV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- RPMTYKAAV was recognized in 7/10 (70%) of individuals with HLA B7, and 0/3 (0%) of individuals with HLA B35. It was a moderate affinity HLA binder.

HXB2 Location Nef (77–85)
Author Location Nef (77–85)
Epitope RPMTYKAAL
Epitope name B7-RL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.

- 3/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.

HXB2 Location Nef (77–85)
Author Location Nef (77–85)
Epitope RPMTYKAAV
Epitope name B7-RV9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 2/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 3/4 individuals had detectable responses to this epitope after STI.

HXB2 Location Nef (77–85)
Author Location Nef (75–83)
Epitope RPMTYKAAL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 3/7 patients recognized this epitope.

HXB2 Location Nef (77–85)
Author Location Nef (75–83)
Epitope RPMTYKGAL
Epitope name RPM
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A02, A68.1, B0702/4/7, B3503, Cw0401, Cw0702, DR17, DR15, DR51, DR52, DQ2, DQ6
Assay type CD8 T-cell Elispot - IFNγ, Tetramer binding, CD4 T-cell Elispot - IFNγ
Keywords rate of progression, immunodominance, escape
References Oxenius *et al.* 2004b

- The increase in plasma viral load in a patient that progressed rapidly was preceded by positive selection of viral escape mutations in epitopes targeted by dominant HIV-1-specific CD8+ T-cell responses,and a decrease in HIV-1-specific CD4+ and CD8+ T-cell frequencies. Overall, escape variant epitopes were recognized 0-80% as efficiently as the index peptide, and the relatively efficiency of the variant eptiopes increased using PBLs collected after their appearance. No changes were found in viral tropism, replication kinetics and neutralizing antibody titers, so the rapid decline of the patient was attributed to loss of HIV containment due to CTL escape.
- This epitope was one of six epitopes found to be under positive selection for escape mutations and was completely replaced by escape variants between days 172 and 635 (rpmtFkgal, rpmSykAal, rpmtykgaV, rpmtykAal). The first two were the most common at day 635, and experimentally shown to be escape.

HXB2 Location Nef (77–91)
Author Location Nef (77–91)
Epitope RPMTYKGAFDLSFFL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Nef (79–87)
Author Location Nef (81–89 HXB3)
Epitope MTYKAALDL
Immunogen Vaccine
Vector/Type: DNA, peptide *Strain:* B clade HXB3 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (A*0201)
Keywords binding affinity, computational epitope prediction
References Sandberg *et al.* 2000

- Ten Nef 9-mer peptides were predicted to have a strong binding affinity with HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly.
- A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with either nef DNA under the control of a CMV promotor coated on, gold particles delivered to abdominal skin by gene gun.
- MTYKAALDL bound weakly to HLA-A2, but the DNA nef vaccine elicited a good CTL response.

HXB2 Location Nef (79–87)
Author Location Nef (79–87)
Epitope MTYKAALDL
Epitope name Nef79-87
Immunogen HIV-1 infection
Species (MHC) human, humanized mouse (A2)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords responses in children, immunodominance, characterizing CD8+ T cell responses
References Chandwani *et al.* 2004

- Responses to five HLA-A2 presented epitopes in Nef were characterized in a population of 19 HIV infected adults and 21 children. The CD8 T-cell response to Nef was stronger and broader in adults than children, averaging 652 and 87 SFCs/10^6 PBMC, and 2.6 and 0.9 recognized epitopes per person, respectively.
- This is one of three novel Nef epitopes previously identified in HLA-A2 transgenic mice, shown to induce CD8 T-cell response in humans. It was not the immunodominant response.

HXB2 Location Nef (80–87)
Author Location Nef (80–87)
Epitope TYKAAVDL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A24)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location Nef (80–94)
Author Location Nef (80–94 HXB2)
Epitope TYKAAVDLSHFLKEK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 47% of the study subjects, and it was the most frequently recognized peptide.

HXB2 Location Nef (82–90)
Author Location (C consensus)
Epitope KGAFDLSFF
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*57)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Nef (82–90)
Author Location Nef (C consensus)
Epitope KAAFDLSFF
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords escape, reversion, viral fitness
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.

- People who carried B57 all carried a variant of this epitope, while about half of the people who did not carry B57 carried the susceptible form, suggesting there is not a high fitness cost and revision rate in this case.
- HLA-B57 was associated with a low viral load.

HXB2 Location Nef (82–91)
Author Location Nef (82–91)
Epitope KAALDLSHFL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A2)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of 31 that the vaccinated volunteers responded to.
- A KAAvDLSHFL variant was cross-recognized after the last boost.

HXB2 Location Nef (82–91)
Author Location Nef (82–91 LAI)
Epitope KAAVDLSHFL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw*0802)
Keywords HAART, ART
References Nixon *et al.* 1999

- A patient who made a mono-specific CTL response to this Nef specific epitope was given effective anti-retroviral therapy within 90 days of infection, reducing the antigenic stimulous.
- Within 7 days of therapy, his CTLp frequency dropped from 60 to 4 per million PBMC, as his viremia dropped.
- The patient went from having an activated effector population (detected by CTLp and clone specific RNA) to a non-activated quiescent population (detected by the CTL-clone specific DNA)

HXB2 Location Nef (82–91)
Author Location Nef (82–91 LAI)
Epitope KAAVDLSHFL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw*0802 (Cw8))
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a C*0802(Cw8) epitope.

HXB2 Location Nef (82–91)
Author Location Nef (82–91 SF2)
Epitope KAAVDLSHFL
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-Cw8+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/0 group 2, and 0/1 group 3.

HXB2 Location Nef (82–91)
Author Location Nef (SF2)
Epitope KAAVDLSHFL
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.

HXB2 Location Nef (82–91)
Author Location (B consensus)
Epitope KAAVDLSHFL
Epitope name KL10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw8)
Donor MHC A25, A32, B08, B14, Cw7, Cw8
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location Nef (82–96)
Author Location Nef (82–96)

Epitope KGAFDLSFFLKEKGG
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Nef (82–101)
Author Location Nef (81–100 SF2)
Epitope KAAVDLSHFLKEKGGLEGLI
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- Three of these 11 had CTL response to this peptide.
- The responding subjects were HLA-A1, A2, B8, B14; HLA-A11, A24, B8, B53.

HXB2 Location Nef (82–101)
Author Location Nef (SF2)
Epitope KAAVDLSHFLKEKGGLEGLI
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2001a

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study.
- Nef peptides PQVPLRRMTYKAAVDLSHFL, KAAVDLSHFLKEKGGLEGLI and EEEEVGFPVTPQVPLRPMTY were recognized and the first two share KAAVDLSHFL (a Cw8 epitope), the first and last share PQVPLRPMTY.

HXB2 Location Nef (83–91)
Author Location Nef (85–93 HXB3)
Epitope AALDLSHFL
Immunogen Vaccine
Vector/Type: DNA, peptide *Strain:* B clade HXB3 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (A*0201)
Keywords binding affinity, computational epitope prediction
References Sandberg *et al.* 2000

- Ten Nef 9-mer peptides were predicted to have strong binding affinity for HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly.
- A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by gene gun.
- AALDLSHFL was predicted to have a strong binding capacity for HLA-A2, and did, but it was the only one of the peptides recognized that was a strong binder, the other two recognized peptides were weak binders.
- AALDLSHFL was also tested by subcutaneous injection of Nef peptides in Freund's adjuvant and gave a strong response to the peptide.

HXB2 Location Nef (83–91)
Author Location Nef (83–91 BRU)
Epitope AAVDLSHFL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- AAVDLSHFL was recognized in 3/18 (17%) of individuals with HLA A2. It was a low affinity HLA binder.

HXB2 Location Nef (83–91)
Author Location Nef (83–91)
Epitope AAVDLSHFL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A2)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of 31 that the vaccinated volunteers responded to.

HXB2 Location Nef (83–91)
Author Location Nef (83–91)
Epitope AALDLSHFL

Epitope name Nef83-91
Immunogen HIV-1 infection
Species (MHC) human, humanized mouse (A2)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords responses in children, immunodominance, characterizing CD8+ T cell responses
References Chandwani *et al.* 2004

- Responses to five HLA-A2 presented epitopes in Nef were characterized in a population of 19 HIV infected adults and 21 children. The CD8 T-cell response to Nef was stronger and broader in adults than children, averaging 652 and 87 SFCs/10^6 PBMC, and 2.6 and 0.9 recognized epitopes per person, respectively.
- The novel AALDLSHFL Nef epitope was the most frequently and most strongly recognized epitope in this study, making it a possible immunodominant epitope.
- This is one of three novel Nef epitopes previously identified in HLA-A2 transgenic mice, shown to induce CD8 T-cell response in humans.

HXB2 Location Nef (83–91)
Author Location Nef (83–91)
Epitope AAVDLSHFL
Immunogen HIV-1 infection
Species (MHC) human (B60, B62, Cw*0802, Cw8)
Donor MHC A*0201, A23, B44, B62, Cw3, Cw4; A1, A3, B7, B14, Cw*0702, Cw*0802; A*0201, A31, B44, B60, Cw3, Cw16; A1, A1, B8, B14, Cw7, Cw8
Assay type CD8 T-cell Elispot - IFNγ
Keywords acute infection, early treatment
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- Four different individuals recognized this epitope during a primary infection, and it was shown to be presented by HLA B60, B62, C2*0802, and Cw8.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location Nef (83–91)
Author Location Nef (83–91)
Epitope AALDLSHFL
Immunogen
Species (MHC) human (Cw*03)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (83–92)
Author Location Nef (81–90 93TH253 subtype CRF01)
Epitope GAFDLSFFLK
Epitope name N83-92
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Sriwanthana *et al.* 2001

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was strongly reactive in HIV+ study subjects 053 and 184 who carried HLA-A11.

HXB2 Location Nef (83–92)
Author Location Nef (81–90 93TH253 subtype CRF01)
Epitope GAFDLSFFLK
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive.
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified.
- This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined.
- 4/8 tested FSWs recognized this epitope.
- This epitope was only conserved in CRF01 and subtype C, and exact matches were uncommon.

HXB2 Location Nef (83–92)
Author Location Nef (83–92)
Epitope AAVDLSHFLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
Donor MHC A*0201, A11, B51, B61, Cw2, Cw14
Assay type CD8 T-cell Elispot - IFNγ

Keywords acute infection, early treatment
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.

HXB2 Location Nef (83–94)
Author Location Nef (83–94 BRU)
Epitope AAVDLSHFLKEK
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Culmann *et al.* 1991

- Epitope defined by boundaries of overlapping peptides that stimulate Nef CTL clones.

HXB2 Location Nef (84–91)
Author Location Nef (84–91)
Epitope AVDLSHFL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A2)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of 31 that the vaccinated volunteers responded to.

HXB2 Location Nef (84–91)
Author Location Nef (84–91 LAI)
Epitope AVDLSHFL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Bw62)
References Culmann-Penciolelli *et al.* 1994

HXB2 Location Nef (84–91)
Author Location Nef (84–91)
Epitope AVDLSHFL
Immunogen HIV-1 infection
Species (MHC) human (Bw62)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope.

HXB2 Location Nef (84–92)
Author Location Nef (84–92)
Epitope AVDLSHFLK
Immunogen HIV-1 infection
Species (MHC) human (A*03)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (84–92)
Author Location Nef (84–92 LAI)
Epitope AVDLSHFLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*1101 epitope.

HXB2 Location Nef (84–92)
Author Location Nef (84–92)
Epitope AVDLSHFLK
Subtype B, CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A*1101)
Keywords inter-clade comparisons
References Fukada *et al.* 2002

- Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals.
- AVDLSHFLK was found to elicit clade-specific responses in clade B (AVDLSHFLK is most common, aLdlshflk is a common variant also found in clade A) and clade E (aFdlsFflk is most common and is also common in clade C). AVDLSHFLK was strongly recognized by CTL from 2/5 B clade infected Japanese subjects, as was aLdlshflk, and aFdlsFflk by CTL from 5/7 E clade infected Thai subjects.

- The binding of aFdlsFflk to HLA A*1101 was 10-50 times lower than the other variants, and bulk CTL generated from individuals did not cross-react with the cross-clade peptides.

HXB2 Location Nef (84–92)
Author Location Nef (84–92 LAI)
Epitope AVDLSHFLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords review
References McMichael & Walker 1994

- Review of HIV CTL epitopes.
- C. Brander notes that this is an A*1101 epitope in the 1999 database.

HXB2 Location Nef (84–92)
Author Location Nef (84–92)
Epitope AVDLSHFLK
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope.

HXB2 Location Nef (84–92)
Author Location Nef (84–92 LAI)
Epitope AVDLSHFLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords review, escape
References Couillin *et al.* 1994; Goulder *et al.* 1997a

- Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location Nef (84–92)
Author Location Nef (84–92 LAI)
Epitope AVDLSHFLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Couillin *et al.* 1995

- Mutations found in this epitope in HLA-A11 positive and negative donors were characterized.

HXB2 Location Nef (84–92)
Author Location Nef (84–92)
Epitope AVDLSHFLK
Epitope name AVD
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- Both of the 2/8 HLA-A11 study subjects recognized this CTL epitope.
- Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197.
- Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up.

HXB2 Location Nef (84–92)
Author Location Nef (82–90)
Epitope AVDLSHFLK
Immunogen HIV-1 infection
Species (MHC) human (A11)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Nef (84–92)
Author Location Nef (84–92 SF2)
Epitope AVDLSHFLK
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 2/2 group 3.

HXB2 Location Nef (84–92)

Author Location Nef (84–92)
Epitope AVDLSHFLK
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A11)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location Nef (84–92)
Author Location Nef
Epitope AVDLSHFLK
Epitope name AVD
Immunogen HIV-1 infection
Species (MHC) human (A11)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location Nef (84–92)
Author Location Nef
Epitope AVDLSHFLK
Subtype A, B, D, F
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human, macaque (A11)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location Nef (84–92)
Author Location Nef (B consensus)
Epitope AVDLSHFLK
Epitope name AK9
Immunogen HIV-1 infection
Species (MHC) human (A11, A3)
Donor MHC A02, A11, B18, B44, Cw5, Cw12; A03, B14, B60, Cw3, Cw7
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, cross-presentation by different HLA, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 2/9 individuals recognized this epitope, each in the context of a different HLA-presenting molecule.

HXB2 Location Nef (84–92)
Author Location Nef (84–92 BRU)
Epitope AVDLSHFLK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- AVDLSHFLK was recognized in 4/12 (33%) of individuals with HLA A3. It was a high affinity HLA-A3 binder.

HXB2 Location Nef (84–92)
Author Location Nef (84–94)
Epitope AVDLSHFLK
Epitope name A3-ALK9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Donor MHC A3, B7, Cw7

Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.

HXB2 Location Nef (84–92)
Author Location Nef (84–92)
Epitope AVDLSHFLK
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A3, A11)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the most frequently recognized of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location Nef (86–94)
Author Location Nef
Epitope DLSHFLKEK
Subtype A, B, D, F
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human, macaque (A*0301)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location Nef (86–94)
Author Location Nef (86–94)
Epitope DLSHFLKEK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A11, A*0301)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- Two of nine patients responded to this peptide with GzB producing cells, while three of the patients responded with IFN-gamma producing cells. Only one patient had both GzB and IFN-gamma responses.

HXB2 Location Nef (86–94)
Author Location Nef (86–94)
Epitope DLSHFLKEK
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A3)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location Nef (86–94)
Author Location Nef (84–92 LAI)
Epitope DLSHFLKEK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3.1)
Keywords review
References McMichael & Walker 1994

- Review of HIV CTL epitopes.

HXB2 Location Nef (86–100)
Author Location Nef (86–100 LAI)

Epitope DLSHFLKEKGGLEGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Robertson *et al.* 1993
- Development of a retroviral vector (pNeoNef) to generate autologous targets.

HXB2 Location Nef (86–100)
Author Location Nef (86–100 LAI)
Epitope DLSHFLKEKGGLEGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Buseyne *et al.* 1993b

HXB2 Location Nef (86–100)
Author Location Nef (86–100 LAI)
Epitope DLSHFLKEKGGLEGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35, Cw4)
References Buseyne *et al.* 1993a
- Vertical transmission of HIV ranges from 13% to 39%
- Primary assays showed that cytotoxic activity against at least one HIV protein was detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study.

HXB2 Location Nef (87–102)
Author Location Nef
Epitope FSHFLKEKGGLEGLIY
Immunogen
Species (MHC) human
Keywords inter-clade comparisons
References Jubier-Maurin *et al.* 1999
- 41 new HIV-1 strains describing envelope subtypes of HIV-1 A-H were genetically characterized in the nef region – 34 subtypes were classified in the same subtype in nef and env and 7 of the 41 strains were recombinants.
- This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes.

HXB2 Location Nef (88–100)
Author Location Nef (103–116)
Epitope SHFLKEKGGLEGL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Guimarães *et al.* 2002
- Nef sequences were obtained from Brazilians to study epitope diversity in this geographic region—most B subtype sequences are SHFLKEKGGLEGL, but sFflkekgglegl is found in most subtype C samples.

HXB2 Location Nef (90–97)
Author Location Nef (89–97)
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Betts *et al.* 2000
- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals that responded to SLYNTVATL reacted with seven other epitopes including this epitope previously described as presented by B8.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords dendritic cells
References Ostrowski *et al.* 2000
- The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*
- Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients.
- Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes.
- The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)

HXB2 Location Nef (90–97)
Author Location
Epitope FLKEKGGL
Epitope name Nef-FL8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*08)
References Sabbaj *et al.* 2002b
- Among HIV+ individuals who carried HLA B*08, 1/3 (33%) recognized this epitope.

HXB2 Location Nef (90–97)
Author Location Nef (89–97 LAI)
Epitope FLKEKGGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*0801 epitope.

HXB2 Location Nef (90–97)
Author Location Nef (90–97)
Epitope FLKEKGGL
Epitope name FL8

Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Donor MHC A*0201, A*2402, B*0801, B*5701, Cw*0602, Cw*0701; A*0101, A*0201, B*0801, B*5701, Cw*0602, Cw*0701; A2, A*2402, B*0801, B15, Cw7, Cw12; A*0101, A*0201, B*0801, B*5701, Cw*0602, Cw*0701
Country United Kingdom.
Assay type CD8 T-cell Elispot - IFNγ, Tetramer binding, Chromium-release assay, Flow cytometric CTL assay
Keywords rate of progression, escape, TCR usage, characterizing CD8+ T cell responses
References Dong *et al.* 2004

- In four donors with delayed disease progression the response to the FL8 Nef epitope was dominated by V-beta-13.2 TCR expressing CTLs with an unusually long CDR3 region. These CTLs were shown to be resistant to apoptosis and able to recognize escape variants of the FL8 Nef epitope. Thus, selection of these CTLs may be related to better clinical outcome.
- The Q5 variant flkeQggl was repidly selected in a donor that reponded to the FLKEKGGL epitope. The FLKEKGGL peptide and the variant flkeQggl HLA-B8 complexes bound to the Vbeta13.2 FLKEKGGL TCR with equal affinity, while the Vbeta6 FLKEKGGL TCR had reduced affinity for the FLKEKGGL form and did not recognize the Q5 variant. Other variants (T5, N5, and M5 as well as Q5) were recognized by Vbeta13.2 clones from all four donors. One clone from donor 046 that was not Vbeta13.2 could only recognize the index variant.

HXB2 Location Nef (90–97)
Author Location (C consensus)
Epitope FLKEKGGL
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*0801)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Nef (90–97)
Author Location Nef (89–97 LAI)
Epitope FLKEKGGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords review, escape
References Price *et al.* 1997

- CTL escape variants appeared over time in HLA-B8 HIV-1 + individual, providing evidence of immune escape.
- Most variants appear at position 5, an anchor residue.
- FLKE(E,N or Q)GGL showed reduced binding efficiency and recognition.
- Double mutants (FIKENGGL, FLEENGGL, and FLKGNGGL) completely escaped recognition.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study in the context of CTL escape to fixation.

HXB2 Location Nef (90–97)
Author Location Nef (90–97 IIIB)
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, responses in children
References Spiegel *et al.* 1999

- Study examines the effect of highly active antiretroviral therapy (HAART) on HIV-1 plasma viral load, CTLp and CTLe frequencies in 8 infected children.
- CTLp (precursors) were measured by stimulating in culture and assaying using 51Cr release, against vaccina expressed IIIB Env, Gag, Pol, Nef.
- B7-FLKEKGGL tetramer complex was used for one of the children that was HLA-B7, and this infant showed a vigorous response ($>$ 4% of CD8+ T cells) at 9 months of age.
- HIV-1 specific CTL responses initially increased in children with complete viral suppression, but then decreased, suggesting viral replication is needed to maintain CTL responses.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Immunogen Vaccine
Vector/Type: vaccinia
Species (MHC) human (B8)
References Hanke *et al.* 1998a; Hanke *et al.* 1998b

- This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans.

HXB2 Location Nef (90–97)
Author Location Nef (88–95)
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Goulder *et al.* 1997g

- Natural variants for this epitope have been observed in several donors.
- Substitutions Q5, N5, E5 that alter anchor position 5 are not well recognized.
- Substitution I2 binds well to B8 and is recognized.

HXB2 Location Nef (90–97)
Author Location Nef (90–97)
Epitope FLKEKGGL

Immunogen HIV-1 infection
Species (MHC) human (B8)
References Dyer *et al.* 1999

- CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective.
- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.

HXB2 Location Nef (90–97)
Author Location Nef (SF2)
Epitope FLKEKGGL
Epitope name FL8
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Goulder *et al.* 2001a

- This peptide elicited a weak CTL response during acute HIV-1 infection in patient PI004.
- Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.
- FL8 was recognized in an additional patient, AC29, in chronic infection.

HXB2 Location Nef (90–97)
Author Location Nef (92–99)
Epitope FLKEKGGL
Epitope name FLK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART
References Oxenius *et al.* 2001a

- Characterization of specific CTL phenotype patterns in response to variation of the virus load in response to antiviral therapy in 3 patients with chronic HIV-1 infection.
- CTL activation in response to increasing viral load sequential, and co-segregated with apoptosis only during later stages of the response, suggesting antigen-specific cell-death is restricted to distinct CTL sub-populations.

HXB2 Location Nef (90–97)
Author Location Nef (92–99)
Epitope FLKEKGGL
Epitope name FLK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI), immunodominance, escape, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- Six of the 7/8 study subjects that were HLA B8 recognized this early dominant CTL epitope.
- Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responsiveness against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII peptides – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones.
- Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQGYFPDWQNY, and GEIYKRWII peptides and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent.
- Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197.
- Patient SC10(HLA A1/3, B8/35, DR1/8, DQ 4/5) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL and a response to GEIYKRWII through day 1088.
- Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy.
- Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640 had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Kostense *et al.* 2001

- HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load.
- Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional.
- In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival.
- Stimulation with HLA-B8 p24 and Nef epitopes significantly increased Nef-specific T-cell numbers in 2 patients (748 and 1113)
- There were more functional IFN-gamma producing Nef-specific T-cells within the T-cell population than there were active p24 Gag-specific T-cells.

- No correlation between elevated numbers of Nef-specific CTL cells and plasma viral load was observed.

HXB2 Location Nef (90–97)
Author Location Nef (88–95)
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Nef (90–97)
Author Location Nef (88–95 SF2)
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/3 group 2, and 1/2 group 3.

HXB2 Location Nef (90–97)
Author Location Nef (89–97)
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Appay *et al.* 2000

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

HXB2 Location Nef (90–97)
Author Location Nef (90–97)
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Day *et al.* 2001

- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.
- The response to FLKEKGGL was the second highest response in magnitude compared to all the HLA class I A- and B-restricted epitopes tested in this individual.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
References Goulder *et al.* 2000b

- Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA])
- HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection.

HXB2 Location Nef (90–97)
Author Location Nef (90–97 BRU)
Epitope FLKEKGGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- FLKEKGGL was recognized in 12/14 (86%) of individuals with HLA B8, and it was a high affinity HLA binder.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Epitope name FLK
Immunogen HIV-1 infection
Species (MHC) human (B8)
Keywords HAART, ART, supervised treatment interruptions (STI)
References Oxenius *et al.* 2002b

- Using previously defined epitopes Oxenius *et al.* [2000, 2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).
- STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.

HXB2 Location Nef (90–97)
Author Location Nef

Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A2, A11, B8, B60, Bw6
Keywords HAART, ART
References Appay *et al.* 2002

- Four HIV patients with prolonged clinically successful antiviral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized FLKEKGGL.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A1, A3, B8, B65, Bw6
Keywords HAART, ART
References Appay *et al.* 2002

- Four HIV patients with prolonged clinically successful antiviral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized FLKEKGGL.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Subtype A, B, C, D
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Species (MHC) human, macaque (B8)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location Nef (90–97)
Author Location Nef (90–97)
Epitope FLKEKGGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A1, A3, B8, B62, Cw3, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location Nef (90–97)
Author Location Nef (90–97 B consensus)
Epitope FLKEKGGL
Epitope name FL8
Subtype B
Immunogen Vaccine
Vector/Type: adeno-associated virus (AAV)
HIV component: gp120
Species (MHC) human (B8)
Assay type Chromium-release assay, Flow cytometric CTL assay
Keywords dynamics, immune evasion
References Brainard *et al.* 2004

- HIV-1 gp120 is shown to suppress the ability of antigen-specific CTLs to migrate or remain at sites of high viral replication by concentration-dependent chemotaxis and fugetaxis.

Directional T-cell movement is shown to depend on the interaction of the V2 and V3 loops with the CXCR4 receptor. X4 HIV-1 gp120 causes the migration of T-cells, including HIV-1 specific CTL, away from infected target cells, another potential mechanism for immune evasion.

HXB2 Location Nef (90–97)
Author Location Nef (87–95)
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A03, A28, B07, B08
Assay type proliferation, Chromium-release assay, Flow cytometric CTL assay
Keywords HAART, ART, memory cells, immune dysfunction
References Gamberg *et al.* 2004a

- HAART restores HIV specific immunity after advanced infection by increase of CD4+ and CD8+ T cell numbers after supression of viral replication. However, HIV specific CTLs emerged only with detectable viral replication breakthroughs and were short-lived while CD4+ T-cell responses remained compromised, suggesting failure of generating stable CD8+ memory T-cells in the absence of HIV-specific T-helper responses.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) (B8)
Keywords binding affinity, review, escape, characterizing CD8+ T cell responses
References da Silva 2003

- Evidence of the evolutionary adaptation of HIV-1 to the specific neutralizing antibody response and CTL detection is reviewed. Both SIV and HIV epitopes are discussed, with a detailed summary of one patient's response and CTL escape in the FLKEKGGL epitope. The three C-terminal amino acids were left unchanged, and it may be due to high fitness costs as these are putatively invloved in CD4 down-regulation and formation of a hydrophobic pocket in Nef. The N terminal residue is involved in binding to protein tyrosine kinases.
- Immediately after infection the susceptible eptiope FLKEKGGL was found in 20/20 viral sequences. Six months later, it was only found in 4/44 sequences. The flkeNggL form was most common, 24/44 cases; it bound poorly to HLA B08 and was poorly recognized by CTL. Two minor variants were found 3/44 times, flkeEggl and flkeQggl; both bound poorly to B08, but the K->Q substitution was still well recognized. A variant flkDkggl was found in 4/44 sequences; it bound B08 moderately well, but was poorly recognized. 3 double mutants were found once each, and were not recognized by CTL: fIkeNggL, flEeNggL, and flkGNggL.

HXB2 Location Nef (90–97)
Author Location Nef (89–97)
Epitope FLKEKGGL
Immunogen HIV-1 infection
Species (MHC) human (B8)
Assay type cytokine production, proliferation, CD8 T-cell Elispot - IFNγ, Tetramer binding, Intracellular cytokine staining, Flow cytometric CTL assay
Keywords HAART, ART, memory cells, characterizing CD8+ T cell responses
References Daniel *et al.* 2004

- CD4+ and CD8+ responses in chronically HIV-1 infected patients on HAART were weak with decreased polyclonality. Only 33% of patients had CD4+ T-cells that could proliferate, and only 22% had HIV-specific CD8+ T-cells T-cell responses, and those rare responses showed low perforin levels and persistent expression of CD27, indicating incomplete differentiation and loss of lytic function.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Epitope name FL8
Immunogen HIV-1 infection
Species (MHC) human (B8)
Country United States.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Tetramer binding
Keywords immunodominance, acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Lichterfeld *et al.* 2004a

- HIV-1 specific CD8+ T-cells in acute and long-term nonprogressive HIV-1 infection show strong ex-vivo proliferative capacities which are rapidly lost in chronic HIV-1 infection. The loss of CD8+ T-cell function is closely linked with the loss of HIV-1 specific, IL2 secreting CD4+ T-cells. The function can be rescued in vitro and in vivo by restoring the specific CD4+ T-cell help.
- Full CD8+ T-cell responses to this epitope were dependent on co-stimulation with a CD4+ T cell dependent epitope from T-cells harvested during acute infection. The CD8+ T-cell response to this epitope was immunodominant in one study individual.

HXB2 Location Nef (90–97)
Author Location (B consensus)
Epitope FLKEKGGL
Epitope name FL8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Donor MHC A02, A03, B08, B62, Cw7, Cw10; A11, A29, B08, B44, Cw4, Cw7; A25, A32, B08, B14, Cw7, Cw8; A01, A03, B08, B14, Cw7, Cw8
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 4/9 individuals recognized this epitope, presented by HLA-B8.

HXB2 Location Nef (90–97)
Author Location Nef
Epitope FLKEKGGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B8)
Country United Kingdom.
Assay type Tetramer binding, T-cell Elispot, Intracellular cytokine staining
Keywords rate of progression, acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Papagno *et al.* 2004

- Acute HIV-1 infection induces massive activation of HIV-specific and non-HIV-specific CD8+ T-cells resulting in differentiation of these cells. High differentiation of CD8+ T-cells is correlated with disease progression. Differentiation is a natural process but it can be driven by elevated immune activation, such as in HIV infection.

HXB2 Location Nef (90–100)
Author Location Nef (90–100 BRU)
Epitope FLKEKGGLEGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- FLKEKGGLEGL was recognized in 8/12 (67%) of individuals with HLA A2. It was a low affinity HLA A2 binder.

HXB2 Location Nef (90–104)
Author Location Nef (90–105 HXB2)
Epitope FLKEKGGLEGLIHSQ
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location Nef (92–100)
Author Location (LAI)
Epitope KEKGGLEGL
Subtype B
Immunogen
Species (MHC) human (B*4001)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4001,B60 epitope.

HXB2 Location Nef (92–100)
Author Location
Epitope KEKGGLEGL
Epitope name Nef-KL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*4002)
Donor MHC A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Patient 01RCH59 was Hispanic, not on HAART, and had a viral load of 5100 and CD4 count of 349 – she also recognized TERQANFL, p2p7p1p6(64-70), HLA-B*4002 and AEWDRVHPV, p24(78-86), HLA-B*4002.
- Among HIV+ individuals who carried HLA B40, 3/5 (60%) recognized this epitope.

HXB2 Location Nef (92–100)

Author Location Nef (92–100)
Epitope KEKGGLEGL
Immunogen
Species (MHC) human (B*4002)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (92–100)
Author Location Nef (90–98 SF2)
Epitope KEKGGLEGL
Immunogen HIV-1 infection
Species (MHC) human (B60)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with preseroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 2/2 group 1, 1/1 group 2, and 0/0 group 3.

HXB2 Location Nef (92–100)
Author Location Nef
Epitope KEKGGLEGL
Immunogen HIV-1 infection
Species (MHC) human (B60)
Keywords epitope processing
References Cao *et al.* 2002

- KM is a B60 restricted CTL clone that recognizes KEKGGLEGL.
- CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.

HXB2 Location Nef (92–100)
Author Location Nef (92–100 NL-43)
Epitope KEKGGLEGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B60)
Keywords class I down-regulation by Nef, escape
References Ali *et al.* 2003

- NL43 was passaged in the presence of Nef KEKGGLEGL-specific CTL clones STD11 and KM3, giving rise to rapid selection of escape mutations, including E93G, E93K, K94N+G99R, G95R+G99R, E98K, E98D, G99R, G99E, L100P, and L100I; insertions, deletions, frameshifts and an early stop codon. 34/36 (94%) of sequences carried mutations in the epitope by seven days, 36/36 (100%) by 14 days.
- NL43 was also passaged in the presence of a Nef TQGYFPDWQNY-specific CTL clone. 7/15 clones had a frameshifting or stop codon introduced by one week; F121T was also observed. The most common escape mutation for both Nef epitopes was an early stop codon at position 91.
- Several mutations selected by KEKGGLEGL-specific CTL were shown to impair the down regulation of class I MHC by Nef, in particular E93G, E93K, and a truncation mutation at position 51.
- Nef deletion mutants increased 100-fold NL-43 susceptibility to inhibition by CTL specific for epitopes in other proteins, the A2 epitopes ILKEPVHGV in RT and SLYNTVATL in p17 Gag.

HXB2 Location Nef (92–100)
Author Location Nef
Epitope KEKGGLEGL
Epitope name KL9
Immunogen HIV-1 infection
Species (MHC) human (B60)
Donor MHC A2, A24, B38, B60, Cw2, Cw12
Assay type CD8 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), early treatment
References Montefiori *et al.* 2003

- HIV-1 + patient AC10 underwent early HAART treatment, which was discontinued 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.

HXB2 Location Nef (92–100)
Author Location Nef (92–100 NL43)
Epitope KEKGGLEGL
Epitope name KL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B60)
Assay type Chromium-release assay, CTL suppression of replication
Keywords escape
References Yang *et al.* 2003a

- Virus was cultured in the presence of CTL lines specific for 5 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, SEGATPQDL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be

monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts.
- Two cloned CTL lines recongized KEKGGEGL, STD11 and KM3. Highly resistant clones emerged after a single round of passage with both CTL clones, and multiple substitutions accrued including frameshits and stop codons, reflecting the dispensability of Nef in viral culture.
- The following epitope variants were observed after passaging with clone STD11 for one week: kekggegI, kKkggegl, and 12/20 frameshifts and 1 early stop. By two weeks, a more complex polyclonal mixture was observed including: kekggegI, kKkggegl kekggegP, kekggeEl, kekggeRl, kekRgeRl, keNggeRl, and 11/22 framshifts.

HXB2 Location Nef (92–100)
Author Location Nef (92–100)
Epitope KEKGGLEGL
Epitope name Nef KL9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B60)
Assay type Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, TCR usage, characterizing CD8+ T cell responses
References Yang *et al.* 2003b

- Killing efficiency of CTLs and their ability to suppress viral replication is shown to depend more on epitope specificity than to antigenic avidity. Different clones recognizing the same epitope had similar killing efficiency despite their variation in avidity. Nef specific CTL clones tended to be most inhibitory, followed by Gag, then by RT specific clones, regardless of avidity.
- 2/14 CTL T-cell clones tested were specific for Nef KL9. Under conditions of excess peptide (100ug/ml), there was no difference in their lytic potential; all possessed similar effector capacity. Avidity was measured as the sensitizing dose of peptide required for 50% of maximal killing (SD50), which varied from 20 pg/ml to 100 ng/ml, over four orders of magnitude for all 14 epitopes. The SD50 range for Nef KL9 was 20-30 pg/ml, both high avidity. These clones were among the most efficient at inhibiting viral replication in the set tested, but because of the general lack of correlation between avidity and viral inhibition efficiency in this study, the authors attribute other reasons to Nefs ability to inhibit viral replication that pertain to presentation like kinetics and expression levels.

HXB2 Location Nef (92–100)
Author Location (B consensus)
Epitope KEKGGLEGL
Epitope name KL10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B60)
Donor MHC A03, B14, B60, Cw3, Cw7
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope; the authors write that it is presented by HLA-B40 in their Table 1, but the subject that recognizes it, AC05, is HLA-B60, so we assume they meant B60.

HXB2 Location Nef (92–100)
Author Location Nef (SF2)
Epitope KEKGGLEGL
Immunogen HIV-1 infection
Species (MHC) human (B60, B*4001)
References Altfeld *et al.* 2000

- This epitope was the dominant B60 (encoded by B*4001) response in 6/8 HLA-B60 individuals, and recognized in all eight.
- This epitope was also recognized two expressing HLA-B61 individuals (B61 is usually encoded by B*4002, but this study did not distinguish between B*4002, B*4003, B*4004, B*4006, and B*4008)
- ELISPOT was a rapid an effective method that was used to define five novel B60 epitopes.
- HLA-B60 is present in 10-20% of the Caucasoid population and B60/B61 are very common in Asian populations.

HXB2 Location Nef (92–100)
Author Location Nef (92–100)
Epitope KEKGGLEGL
Immunogen HIV-1 infection
Species (MHC) human (B60, B61)
Keywords immunodominance
References Day *et al.* 2001

- No immunodominant responses were detected to five B61-restricted epitopes tested.
- All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response.

HXB2 Location Nef (92–112)
Author Location Nef (SF2)
Epitope KEKGGLEGLIHSQRRQDILDL
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.
- The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.

HXB2 Location Nef (92–112)

Author Location Nef (SF2)
Epitope KEKGGLEGLIHSQRRQDILDL
Immunogen HIV-1 infection
Species (MHC) human
References Altfeld *et al.* 2000

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.
- The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.

HXB2 Location Nef (93–106)
Author Location Nef (93–106 BRU)
Epitope EKGGLEGLIHSQRR
Immunogen HIV-1 infection
Species (MHC) human (A1, B8)
References Hadida *et al.* 1992

- HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.

HXB2 Location Nef (97–111)
Author Location Nef (97–111)
Epitope LEGLIYSKKRQEILD
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Nef (102–115)
Author Location Nef (102–115 LAI)
Epitope HSQRRQDILDLWIY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords review, escape
References Goulder *et al.* 1997e; Goulder *et al.* 1997a

- HLA identical sibling hemophiliac brothers were both infected with the same batch of factor VIII.
- They were tested 6-8 years after infection; one had a strong response to this peptide, the other did not.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location Nef (102–115)
Author Location Nef (100–113)
Epitope HSQRRQDILDLWIY
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/7 patients recognized this epitope.

HXB2 Location Nef (102–121)
Author Location Nef (101–120 SF2)
Epitope HSQRRQDILDLQIYHTQGYF
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- Two of these 11 had CTL response to this peptide.
- The responding subjects were HLA-A2, A3, B8, B62 and HLA-A2, B21.

HXB2 Location Nef (103–127)
Author Location Nef (103–127 PV22)
Epitope SQRRQDILDLWIYHTQGYFPDWQNY
Immunogen HIV-1 infection
Species (MHC) human (B13)
References Jassoy *et al.* 1993

- HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.

HXB2 Location Nef (103–127)
Author Location Nef (103–127)
Epitope SQRRQDILDLWIYHTQGYFPDWQNY
Epitope name SQR
Immunogen HIV-1 infection
Species (MHC) human (B13)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- The only study subject out of eight that was HLA B13+ recognized this epitope.
- Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQGYFPDWQNY, and GEIYKRWII peptides and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent.

HXB2 Location Nef (105–114)
Author Location Nef (105–114 LAI)

Epitope RRQDILDLWI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*2705)
Keywords rate of progression
References Goulder *et al.* 1997c

- Defined as optimal epitope from within reactive peptide HSQRRQDILDLWIYHTQGYF [Nef(102-121 LAI)]
- HLA-B*2705 is associated with slow HIV disease progression.
- The HLA-B*2705 binding motif includes R at position 2, and L in the C-term position.

HXB2 Location Nef (105–114)
Author Location Nef (105–114 LAI)
Epitope RRQDILDLWI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*2705)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*2705 epitope.

HXB2 Location Nef (105–114)
Author Location Nef (105–114 SF2)
Epitope RRQDILDLWI
Immunogen HIV-1 infection
Species (MHC) human (B27)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B27+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/1 group 3.

HXB2 Location Nef (105–114)
Author Location Nef (105–114)
Epitope RRQDILDLWI
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Day *et al.* 2001

- B27-restricted CTL response was strongest to this epitope in one individual.

HXB2 Location Nef (105–114)
Author Location
Epitope RRQDILDLWI
Epitope name Nef-RI10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B27)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B27, 1/2 (50%) recognized this epitope.

HXB2 Location Nef (105–115)
Author Location Nef (105–115)
Epitope KRQEILDLWVY
Immunogen
Species (MHC) human (Cw*07)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (105–115)
Author Location Nef (105–115)
Epitope RRQDILDLWIY
Immunogen
Species (MHC) human (Cw*07)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (105–115)
Author Location (C consensus)
Epitope KRQEILDLWVY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (Cw*0701, Cw*0702)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Nef (105–115)
Author Location Nef (105–115)
Epitope RRQDILDLWIY
Epitope name Cw7-RY11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- AC-06 was homozygous at all three class I alleles (A3, B7, Cw7), and was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 response to RRQDILDLWIY restricted by HLA-Cw7.

HXB2 Location Nef (105–115)
Author Location Nef (C consensus)
Epitope KKQEILDLWVY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (Cw7)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords escape
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- People who carried Cw07 often carried a variant of this epitope, while the susceptible form of the epitope waas highly conserved among those who did not.

HXB2 Location Nef (105–119)
Author Location Nef (105–119 HXB2)
Epitope RRQDILDLWIYHTQG
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location Nef (106–115)
Author Location (LAI)
Epitope RQDILDLWIY
Subtype B
Immunogen
Species (MHC) (B7)
Keywords optimal epitope
References Frahm *et al.* 2004; Goulder 1999

HXB2 Location Nef (108–115)
Author Location
Epitope DILDLWIY
Epitope name Nef-DY8
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Cw*0701)
Donor MHC A*3303 A*2601 B*5801 B*8201 Cw*0302 Cw*0701
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subject 03RCH40 was African American, had a viral load of 2500, CD4 count of 372, was not on HAART, and also recognized the epitope ETKLGKAGY, RT(449-457), A*2601.
- Among HIV+ individuals who carried HLA Cw07, 2/18 (11%) recognized this epitope.

HXB2 Location Nef (108–115)
Author Location Nef (108–115)
Epitope DILDLWIY
Immunogen HIV-1 infection
Species (MHC) human (Cw7)
Donor MHC A1, A1, B8, B14, Cw7, Cw8
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.

- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

HXB2 Location Nef (112–126)
Author Location Nef (112–126)
Epitope LWVYHTQGYFPDWQN
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Nef (112–133)
Author Location Nef (111–132)
Epitope LWIYHTQGYFPDWQNYTPGPGV
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location Nef (112–133)
Author Location Nef (111–132 SF2)
Epitope LWIYHTQGYFPDWQNYTPGPGV
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- Four of these 11 had CTL response to this peptide.
- The responding subjects were HLA-A2, B21; HLA-A1, A3, B7, B15; HLA-A2, A26, B7, B38.

HXB2 Location Nef (112–133)
Author Location Nef (111–132 SF2)
Epitope LWIYHTQGYFPDWQNYTPGPGV
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location Nef (113–121)
Author Location Nef (111–119)
Epitope WIYHTQGYF
Immunogen HIV-1 infection
Species (MHC) human (A1)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 3/13 patients recognized this epitope.

HXB2 Location Nef (113–125)
Author Location Nef (113–125 BRU)
Epitope WIYHTQGYFPDWQ
Immunogen HIV-1 infection
Species (MHC) human (B17)
References Culmann *et al.* 1989

- Nef CTL clones from HIV+ donors.

HXB2 Location Nef (113–127)
Author Location Nef (128–142)
Epitope WIYHTQGYFDPWQNY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Guimaráes *et al.* 2002

- Nef sequences were obtained from Brazilians to study epitope diversity in this geographic region – WIYHTQGYFDPWQNY displayed an (H) to (N) substitution in Brazilian Nef-gene subtype C samples, and this substitution is often found in other subtypes tested.

HXB2 Location Nef (113–128)
Author Location Nef (113–128 BRU)
Epitope WIYHTQGYFPDWQNYT
Immunogen HIV-1 infection
Species (MHC) human (A1)
References Hadida *et al.* 1992

- HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.

HXB2 Location Nef (113–128)
Author Location Nef (113–128 LAI)
Epitope WIYHTQGYFPDWQNYT
Epitope name N2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A1)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location Nef (114–127)
Author Location Nef
Epitope VYHTQGYFPDWQNY
Immunogen HIV-1 infection
Species (MHC) human
References Jubier-Maurin *et al.* 1999

HXB2 Location Nef (115–125)
Author Location Nef (115–125 BRU)
Epitope YHTQGYFPDWQ
Immunogen HIV-1 infection
Species (MHC) human (B17)
References Culmann *et al.* 1991
- Nef CTL clones from HIV+ donors.

HXB2 Location Nef (115–129)
Author Location Nef (115–129 HXB2)
Epitope YHTQGYFPDWQNYTP
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003
- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 22% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location Nef (116–124)
Author Location Nef (116–124)
Epitope HTQGYFPDW
Immunogen
Species (MHC) human (B*57)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (116–124)
Author Location Nef (116–124)
Epitope HTQGYFPDW
Immunogen
Species (MHC) human (B*57)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (116–124)
Author Location
Epitope HTQGYFPDW
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement, epitope processing
References Draenert *et al.* 2004a
- 96% of optimally defined epitopes have one of only nine amino acids serving as the C-terminal anchor position. Seven amino acids are never found in this position and four are only present in 4% of cases. CD8 T-cell response to an epitope is shown to be best detected when the epitope is situated at the C-terminal end of a longer peptide, and authors suggest that Elispot reagents would be better designed if peptides ended on known C-terminal anchors.
- HTQGYFPDW is suggested to be the optimal epitope instead of HTQGYFPDWQ since Gln is not described as a C-terminal anchor residue in any of the other optimally defined epitopes. HTQGYFPDW was also found to be recognized at two times lower peptide concentrations than HTQGYFPDWQ.

HXB2 Location Nef (116–125)
Author Location Nef (116–125 BRU)
Epitope HTQGYFPDWQ
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords inter-clade comparisons, optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is a B*5701 epitope.
- Subtype of B57 not determined.

HXB2 Location Nef (116–125)
Author Location Nef (116–125)
Epitope HTQGYFPDWQ
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords immunodominance

References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- One of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others.

HXB2 Location Nef (116–125)
Author Location Nef (116–125 BRU)
Epitope HTQGYFPDWQ
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Culmann *et al.* 1991

- Nef CTL clones from HIV+ donors, optimal peptide mapped.

HXB2 Location Nef (116–125)
Author Location Nef (116–125)
Epitope HTQGYFPDWQ
Epitope name HTQ
Immunogen HIV-1 infection
Species (MHC) human (B57)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- None of the 8 study subjects recognized this epitope but none were HLA B57+

HXB2 Location Nef (116–125)
Author Location
Epitope HTQGYFPDWQ
Epitope name Nef-HQ10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B57, 0/5 (0%) recognized this epitope.

HXB2 Location Nef (116–125)
Author Location Nef (114–123)
Epitope HTQGYFPDWQ
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 7 patients recognized this epitope.

HXB2 Location Nef (117–127)
Author Location Nef (117–127)
Epitope TQGYFPDWQNY
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- 1/11 of the A2+ individuals was HLA A*0205/A*0208, A30, B27, B44 but responded to HLA Bw62 epitope TQGYFPDWQNY, and one of the other individuals that was A2+, but otherwise of unknown HLA type, reacted with seven epitopes including this one.

HXB2 Location Nef (117–127)
Author Location Nef (117–127 LAI)
Epitope TQGYFPDWQNY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1501)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*1501 epitope.

HXB2 Location Nef (117–127)
Author Location Nef (117–127 NL-43)
Epitope TQGYFPDWQNY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1501)
Keywords class I down-regulation by Nef, escape
References Ali *et al.* 2003

- NL43 was passaged in the presence of Nef KEKGGLEGL-specific CTL clones STD11 and KM3, giving rise to rapid selection of escape mutations, including E93G, E93K, K94N+G99R, G95R+G99R, E98K, E98D, G99R, G99E, L100P, and L100I; insertions, deletions, frameshifts and an early stop codon. 34/36 (94%) of sequences carried mutations in the epitope by seven days, 36/36 (100%) by 14 days.
- NL43 was also passaged in the presence of a Nef TQGYFPDWQNY-specific CTL clone. 7/15 clones had a frameshifting or stop codon introduced by one week; F121T was also observed. The most common escape mutation for both Nef epitopes was an early stop codon at position 91.
- Several mutations selected by KEKGGLEGL-specific CTL were shown to impair the down regulation of class I MHC by Nef, in particular E93G, E93K, and a truncation mutation at position 51.

- Nef deletion mutants increased 100-fold NL-43 susceptibility to inhibition by CTL specific for epitopes in other proteins, the A2 epitopes ILKEPVHGV in RT and SLYNTVATL in p17 Gag.

HXB2 Location Nef (117–127)
Author Location Nef (117–127)
Epitope TQGYFPDWQNY
Immunogen HIV-1 infection
Species (MHC) human (B62)
Keywords immunodominance
References Day *et al.* 2001

- No immunodominant responses were detected to four B62-restricted epitopes tested.

HXB2 Location Nef (117–127)
Author Location Nef (117–127 LAI)
Epitope TQGYFPDWQNY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (Bw62)
References Culmann 1998

- Optimal peptide defined by titration.

HXB2 Location Nef (117–128)
Author Location Nef (117–128 BRU)
Epitope TQGYFPDWQNYT
Immunogen HIV-1 infection
Species (MHC) human (B17, B37)
References Culmann *et al.* 1991

- Nef CTL clones from HIV+ donors.

HXB2 Location Nef (117–147)
Author Location Nef (117–147 LAI)
Epitope TQGYFPDWQNYTPGPGVRYPLTFGWCYKLVP
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 1/10 reacted to this Nef peptide.
- 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual.
- 10/12 tested had an IgG response to this peptide.

HXB2 Location Nef (118–127)
Author Location Nef (118–127 LAI)
Epitope QGYFPDWQNY
Subtype B
Immunogen
Species (MHC) human (Bw62)
Keywords review
References McMichael & Walker 1994

- Review of HIV CTL epitopes.

HXB2 Location Nef (120–127)
Author Location (C consensus)
Epitope YFPDWQNY
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*3002, A*29)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Nef (120–127)
Author Location
Epitope YFPDWQNY
Immunogen HIV-1 infection
Species (MHC) human (A29)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords assay standardization/improvement, epitope processing
References Draenert *et al.* 2004a

- 96% of optimally defined epitopes have one of only nine amino acids serving as the C-terminal anchor position. Seven amino acids are never found in this position and four are only present in 4% of cases. CD8 T-cell response to an epitope is shown to be best detected when the epitope is situated at the C-terminal end of a longer peptide, and authors suggest that Elispot reagents would be better designed if peptides ended on known C-terminal anchors.
- Instead of YFPDWQNYT, YFPDWQNY was found to be the optimal epitope in one patient.

HXB2 Location Nef (120–128)
Author Location Nef (120–128)
Epitope YFPDWQNYT
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Betts *et al.* 2000

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.

- 1/11 of the A2+ individuals was HLA A*0205/A*0208, A30, B27, B44 but responded to HLA B37 epitope IYKRWIILGL, and one of the other individuals that was A2+, but otherwise of unknown HLA type, reacted with seven epitopes including this one.

HXB2 Location Nef (120–128)
Author Location Nef (120–128)
Epitope YFPDWQNYT
Immunogen HIV-1 infection
Species (MHC) human (A*29)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (120–128)
Author Location Nef (118–126 SF2)
Epitope YFPDWQNYT
Immunogen HIV-1 infection
Species (MHC) human (A1)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A1+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/2 group 2, and 1/2 group 3.

HXB2 Location Nef (120–128)
Author Location Nef (120–128 LAI)
Epitope YFPDWQNYT
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*3701)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*3701 and B*5701 epitope.

HXB2 Location Nef (120–128)
Author Location Nef (120–128 LAI)
Epitope YFPDWQNYT
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5701)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*5701 epitope.
- Subtype of B57 not determined.

HXB2 Location Nef (120–128)
Author Location Nef (120–128 IIIB)
Epitope FFPDWKNYT
Immunogen HIV-1 infection
Species (MHC) human (B15)
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1999a

- This study describes maternal CTL responses in the context of mother-to-infant transmission.
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants.
- LFPDWKNYT is an escape mutant.

HXB2 Location Nef (120–128)
Author Location Nef (120–128 LAI)
Epitope YFPDWQNYT
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B37, B57)
References Culmann 1998

- Nef CTL clones from HIV+ donors – optimum peptide mapped by titration.

HXB2 Location Nef (120–128)
Author Location Nef (120–128)
Epitope FFPDWKNYT
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 5 epitopes from this individual that varied over time where the internal mutations became fixed; a dramatic decrease in CTL activity against the wild type epitope was observed as the mutation arose. YfpdwQnyt and YfpdwHnyt variants found at 2 months postseroconversion (psc); YfpdwHnyt, YfpdwQSyt, YLpdwQSyt and YfpdwDnyt variants found 20 months psc; YfpdwDnyt and YfpdwQSyt variants found 47 months psc.

HXB2 Location Nef (120–128)
Author Location
Epitope YFPDWQNYT
Epitope name Nef-YT9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B57, 1/5 (20%) recognized this epitope.

HXB2 Location Nef (120–144)
Author Location Nef (120–144 SF2)
Epitope YFPDWQNYTPGPGIRYPLTFGWCYK
Immunogen HIV-1 infection
Species (MHC) human (A24)
References Jassoy *et al.* 1992

- Epitope recognized by CTL clone derived from CSF.

HXB2 Location Nef (121–128)
Author Location Nef (121–128)
Epitope FPDWQNYT
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A1)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of 31 that the vaccinated volunteers responded to.

HXB2 Location Nef (122–136)
Author Location Nef (122–136)
Epitope PDWQNYTPGPGVRYP
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Nef (122–141)
Author Location Nef (121–140 SF2)
Epitope PDWQNYTPGPGVRYPLTFGW
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- Three of these 11 had CTL response to this peptide.
- The responding subjects were HLA-A2, B21; HLA-A3, A24, B7, B38.

HXB2 Location Nef (123–137)
Author Location Nef (123–137 IIIB)
Epitope QWQNYTPGPGVRYPL
Immunogen HIV-1 infection
Species (MHC) human
Keywords responses in children, mother-to-infant transmission, escape
References Wilson *et al.* 1996

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.
- FFPDYTPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants, were found in mother and are not recognized.
- LFPDYKPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants, were found in infant and are not recognized.

HXB2 Location Nef (126–135)
Author Location Nef (126–135 BRU)
Epitope NYTPGPGVRY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A24)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- NYTPGPGVRY was recognized in 3/10 (30%) of individuals with HLA A24. It was a moderate affinity HLA-A24 binder.

HXB2 Location Nef (126–138)
Author Location Nef (126–138 BRU)
Epitope NYTPGPGVRYPLT
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Culmann *et al.* 1991

- Nef CTL clones from HIV+ donors.

HXB2 Location Nef (127–141)
Author Location Nef (127–141)
Epitope YTPGPGVRYPLTFGW
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Novitsky *et al.* 2002

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

HXB2 Location Nef (128–135)
Author Location Nef (128–135 LAI)
Epitope TPGPGVRY
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (B*0702)
Keywords epitope processing
References Lucchiari-Hartz *et al.* 2000

- Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152.
- All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments.
- Both TPGPGVRYPL and TPGPGVRY are naturally processed ligands that can be eluted from HLA-B7 molecules, both are recognized by the same CTL, and both peptides seem to be the direct product of a proteasomal digest.
- The peptide TPGPGVRY is present in a high copy number, TPGPGVRYPL at a more moderate level, possibly due to a major cleavage site between the Y and P.

HXB2 Location Nef (128–135)
Author Location Nef (128–135)
Epitope TPGPGVRY
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B7 supertype)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location Nef (128–136)
Author Location
Epitope TPGPGVRYP
Epitope name Nef-TP9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA B07, 4/9 (44%) recognized this epitope.

HXB2 Location Nef (128–137)
Author Location Nef
Epitope TPGPGIRYPL
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was recognized by 1/22 HEPS control sex workers, ML851.

HXB2 Location Nef (128–137)
Author Location Nef (128–137 LAI)
Epitope TPGPGVRYPL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*0702)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*0702 epitope.

HXB2 Location Nef (128–137)
Author Location Nef (128–137 LAI)
Epitope TPGPGVRYPL
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (B*0702)
Keywords epitope processing
References Lucchiari-Hartz *et al.* 2000

- Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152.
- All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments.
- Both TPGPGVRYPL and TPGPGVRY are naturally processed ligands that can be eluted from HLA-B7 molecules, both are recognized by the same CTL, and both peptides seem to be the direct product of a proteasomal digest.
- The peptide TPGPGVRY is present in a high copy number, TPGPGVRYPL at a more moderate level, possibly due to a major cleavage site between the Y and P.

HXB2 Location Nef (128–137)
Author Location Nef (128–137 LAI)
Epitope TPGPGVRYPL
Subtype B
Immunogen
Species (MHC) human (B*4201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*4201 epitope.

HXB2 Location Nef (128–137)
Author Location (C consensus)
Epitope TPGPGVRYPL

Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B*4201, B*0702)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Nef (128–137)
Author Location Nef (128–137 BRU)
Epitope TPGPGVRYPL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- TPGPGVRYPL was recognized in 8/16 (50%) of individuals with HLA B7, and 1/9 (11%) of individuals with HLA B35. It was a high affinity HLA binder.

HXB2 Location Nef (128–137)
Author Location
Epitope TPGPGVRYPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords acute infection
References Wilson *et al.* 2000a

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

HXB2 Location Nef (128–137)
Author Location Nef (128–137 LAI)
Epitope TPGPGVRYPL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Haas *et al.* 1996; Haas *et al.* 1997

- There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection.
- The epitope position was taken from Haas *et al.* [1997]

HXB2 Location Nef (128–137)
Author Location Nef
Epitope TPGPGVRYPL
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B7)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The D subtype consensus is identical to the B clade epitope.
- The A subtype consensus is TPGPGIRYPL.

HXB2 Location Nef (128–137)
Author Location Nef (subtype B)
Epitope TPGPGVRYPL
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B7)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.

- This epitope is conserved among B and D clade viruses.
- The Clade A version of the epitope: TPGPGIRYPL.

HXB2 Location Nef (128–137)
Author Location Nef (128–137)
Epitope TPGPGVRYPL
Immunogen in vitro stimulation or selection
Species (MHC) human (B7)
Keywords immunodominance, dendritic cells, Th1
References Wilson *et al.* 1999b

- Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors.
- Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within.
- CTL from a B7 donor displayed no reactivity to this epitope, although it had been immunodominant in another study Haas *et al.* [1996]

HXB2 Location Nef (128–137)
Author Location Nef (128–137 SF2)
Epitope TPGPGVRYPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3.

HXB2 Location Nef (128–137)
Author Location Nef (128–137)
Epitope TPGPGVRYPL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B7)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B7 women, 4/5 HEPS and 5/6 HIV-1 infected women recognized this epitope.
- The dominant response to this HLA allele was to this epitope in 3 of the 4/5 HEPS cases and in 2 of the 5/6 HIV-1 infected women.
- Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPG(V/I)RYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.

HXB2 Location Nef (128–137)
Author Location Nef (128–137)
Epitope TPGPGVRYPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Appay *et al.* 2000

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.
- HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

HXB2 Location Nef (128–137)
Author Location Nef (128–137)
Epitope TPGPGVRYPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.

- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

HXB2 Location Nef (128–137)
Author Location Nef (128–137 BRU)
Epitope TPGPGVRYPL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- TPGPGVRYPL was recognized in 8/16 (50%) of individuals with HLA B7, and 1/9 (11%) of individuals with HLA B35. It was a high affinity HLA binder.

HXB2 Location Nef (128–137)
Author Location Nef
Epitope TPGPGVRYPL
Epitope name B7-TL10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A3, B7, Cw7
Keywords dynamics, supervised treatment interruptions (STI), acute infection
References Yu *et al.* 2002a

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.

HXB2 Location Nef (128–137)
Author Location Nef
Epitope TPGPGVRYPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A2, A3, B7, Bw6
Keywords HAART, ART
References Appay *et al.* 2002

- Four HIV patients with prolonged clinically successful antiviral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

HXB2 Location Nef (128–137)
Author Location Nef
Epitope TPGPGVRYPL
Subtype B, C
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade
HIV component: p17 Gag, p24 Gag
Species (MHC) human, macaque (B7)
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location Nef (128–137)
Author Location Nef
Epitope TPGPGVRYPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Koning *et al.* 2004

- A high-risk seronegative group of 29 homosexual men showed reduced cellular in vitro susceptibility for HIV infection and enhanced production of RANTES compared to 15 men who went on to seroconvert. Significantly higher frequencies of HLA A*11, A*31 and Cw*15 were also found in the high risk seronegative men. Both groups of men had low frequencies

of HIV-1 specific CD8+ T-cells, which may signify exposure more than protection from infection.
- No one, 0/9 HLA B7+ infection-resistant men, and 0/4 pre-seroconversion men who went on to become infected, reacted to this epitope.

HXB2 Location Nef (128–137)
Author Location Nef (126–135)
Epitope TPGPGVRYPL
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 6/7 patients recognized this epitope, it was the most commonly recognized of 11 B*07 epitopes.

HXB2 Location Nef (128–137)
Author Location (B consensus)
Epitope TPGPGVRYPL
Epitope name TL10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Donor MHC A31, A68, B07, B70, Cw7, Cw1
Country United States.
Assay type cytokine production, Intracellular cytokine staining, Chromium-release assay, Flow cytometric CTL assay
Keywords assay standardization/improvement, memory cells, characterizing CD8+ T cell responses
References Lichterfeld *et al.* 2004c

- Using a flow-cytometric cytotoxicity assay based on caspase-3 activation in dying target cells, it was shown that the subset of HIV-1-specific CD8+ T-cells secreting both IFN-gamma and TNF-alpha exibit stronger cytotoxic activity than those secreting only IFN-gamma. These cells also exhibited stronger intracellular perforin expression. No association between HIV-1-specific CD8+ T-cell maturation phenotypes and intracellular perforin expression was found.
- 1/9 individuals recognized this epitope.

HXB2 Location Nef (128–137)
Author Location Nef
Epitope TPGPGVRYPL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Country United Kingdom.
Assay type Tetramer binding, T-cell Elispot, Intracellular cytokine staining
Keywords rate of progression, acute infection, characterizing CD8+ T cell responses, immune dysfunction
References Papagno *et al.* 2004

- Acute HIV-1 infection induces massive activation of HIV-specific and non-HIV-specific CD8+ T-cells resulting in differentiation of these cells. High differentiation of CD8+ T-cells is correlated with disease progression. Differentiation is a natural process but it can be driven by elevated immune activation, such as in HIV infection.

HXB2 Location Nef (128–137)
Author Location Nef (128–137)
Epitope TPGPGVRYPL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B7 supertype)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location Nef (128–137)
Author Location Nef (128–137 subtype B)
Epitope TPGPGVRYPL
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B7, B*8101)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location Nef (128–137)
Author Location Nef (subtype B)
Epitope TPGPGVRYPL
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B7, B*8101)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- Clade A version of the epitope: TPGPGIRYPL, clade D version: TPGPGIRYPL.

HXB2 Location Nef (130–139)
Author Location Nef (130–139 BRU)
Epitope GPGVRYPLTF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- GPGVRYPLTF was recognized in 0/10 (0%) of individuals with HLA B7, and 1/11 (9%) of individuals with HLA B35, although it was a high affinity HLA binder.

HXB2 Location Nef (130–143)
Author Location Nef (130–143 LAI)
Epitope GPGVRYPLTFGWCY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*57)
References Goulder *et al.* 1996b

- CTL response to this epitope observed in 4 long-term survivors.
- Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations.

HXB2 Location Nef (130–143)
Author Location Nef (121–141)
Epitope GPGVRYPLTFGWCY
Immunogen HIV-1 infection
Species (MHC) human (B57)
References Ferrari *et al.* 2000

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.

HXB2 Location Nef (130–143)
Author Location Nef (128–141)
Epitope GPGVRYPLTFGWCY
Immunogen HIV-1 infection
Species (MHC) human (B57)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 7/7 patients recognized this epitope.

HXB2 Location Nef (130–144)
Author Location Nef (130–144 HXB2)
Epitope GPGVRYPLTFGWCYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type T-cell Elispot
Keywords supervised treatment interruptions (STI), immunodominance, early treatment
References Addo *et al.* 2003

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 24% of the study subjects, and it was one of the 25 most frequently recognized peptides.

HXB2 Location Nef (132–144)
Author Location Nef
Epitope GIRYPLTFGWCFK
Immunogen
Species (MHC) human
Keywords inter-clade comparisons
References Jubier-Maurin *et al.* 1999

- 41 new HIV-1 strains describing envelope subtypes of HIV-1 A-H were genetically characterized in the nef region – 34 subtypes were classified in the same subtype in nef and env and 7 of the 41 strains were recombinants.
- This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes.

HXB2 Location Nef (132–147)
Author Location Nef (132–147 BRU)
Epitope GVRYPLTFGWCYKLVP
Immunogen HIV-1 infection
Species (MHC) human (A1, B8)
References Hadida *et al.* 1992
- HIV-1 specific CTLs detected in lymphoid organs.

HXB2 Location Nef (132–147)
Author Location Nef (132–147 BRU)
Epitope GVRYPLTFGWCYKLVP
Immunogen HIV-1 infection
Species (MHC) human (B18)
References Culmann *et al.* 1991
- Nef CTL clones from HIV+ donors.

HXB2 Location Nef (132–147)
Author Location Nef (132–147)
Epitope GVRYPLTFGWCYKLVP
Immunogen Vaccine
Vector/Type: DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18
Species (MHC) mouse (H-2^d)
Keywords Th1
References Billaut-Mulot *et al.* 2001
- DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization.
- Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost.
- Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-gamma)
- Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.

HXB2 Location Nef (133–141)
Author Location Nef (133–141)
Epitope TRYPLTFGW
Immunogen HIV-1 infection
Species (MHC) human (A*3303)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (133–148)
Author Location Nef (133–148 LAI)
Epitope VRYPLTFGWCYKLVPV
Subtype B
Immunogen
Species (MHC) human (B57)
References Brander & Walker 1996
- P. Goulder, pers. comm.

HXB2 Location Nef (134–141)
Author Location (C consensus)
Epitope RYPLTFGW
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (A*2301)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004
- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Nef (134–141)
Author Location Nef (138–147 LAI)
Epitope RYPLTFGW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
Keywords optimal epitope
References Frahm *et al.* 2004
- C. Brander notes this is an A*2402 epitope.

HXB2 Location Nef (134–141)
Author Location Nef (138–147 SF2)
Epitope RYPLTFGW
Immunogen HIV-1 infection
Species (MHC) human (A24)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b
- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A24+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 2/3 group 2, and 0/0 group 3.

HXB2 Location Nef (134–141)
Author Location Nef
Epitope RYPLTFGW
Epitope name A24-RW8(Nef)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A24)
Donor MHC A24, A?, B7, B27

Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).

HXB2 Location Nef (134–141)
Author Location Nef (134–141)
Epitope RYPLTFGW
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A33)
Donor MHC A3, A33, B14, B35, Cw*0401, Cw*0802
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location Nef (134–141)
Author Location Nef (134–141 LAI)
Epitope RYPLTFGW
Subtype B
Immunogen
Species (MHC) human (B27)
References Culmann 1998

- Optimal peptide defined by titration.

HXB2 Location Nef (134–143)
Author Location Nef (138–147 SF2)
Epitope RYPLTFGWCF
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
References Ikeda-Moore *et al.* 1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 3/4 HIV-1 + people tested.
- RYPLTFGWCF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

HXB2 Location Nef (134–143)
Author Location Nef (138–147)
Epitope RYPLTFGWCF
Epitope name Nef138-10
Subtype B
Immunogen Vaccine
Vector/Type: Sendai virus vector system (SeV)
Species (MHC) human (A*2402)
References Kawana-Tachikawa *et al.* 2002

- A Sendai virus vector system (SeV) was developed that expressed HLA-A*2402-restricted class I/peptide complexes; this system could be used to detect responses and has the potential to elicit immune responses.
- MHC class I/peptide tetramers could be made using this system that bound to epitope-specific CTLs in PBMCs.
- Cells transfection with SeV modified to express A*2402-HIV epitope complexes induced CTL mediated specific cell lysis.

HXB2 Location Nef (134–143)
Author Location Nef
Epitope RYPLTFGWCF
Epitope name Nef138-10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*2402)
Donor MHC A*2402
Country Japan.
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay

Keywords binding affinity, epitope processing, immunodominance, escape
References Furutsuki *et al.* 2004

- 70% of Japanese people carry HLA A*2402, and the rFpltfgwcf (2F) escape variant of this A*2402 epitope was found to be positively selected in Japan; reversion to wild-type in HLA-A24 negative individuals occurred very slowly over years. The 2F escape variant appears to be common in Japan due to escape and then transmission of this form in the population. The mechanism of escape appeared to be in processing of Nef and antigen presentation rather than HLA binding since both wild-type and 2F variant bound to HLA-A*2402 with almost same efficiency; the authors suggest the epitope may be cleaved at position 5 with a higher frequency when the 2F mutation is present.

HXB2 Location Nef (134–143)
Author Location Nef (134–143 BRU)
Epitope RYPLTFGWCY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A24)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- RYPLTFGWCY was recognized in 5/12 (42%) of individuals with HLA A24. It was a moderate affinity HLA-A24 binder.

HXB2 Location Nef (134–143)
Author Location Nef (134–143)
Epitope RYPLTFGWCY
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A24)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location Nef (134–144)
Author Location Nef (134–144 LAI)
Epitope RYPLTFGWCYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B18)
Keywords review, escape
References Couillin *et al.* 1994; Goulder *et al.* 1997a

- Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response.
- Goulder *et al.* [1997a] is a review of immune escape that summarizes this study.

HXB2 Location Nef (134–144)
Author Location Nef (134–144)
Epitope RYPLTFGWCYK
Epitope name RYP
Immunogen HIV-1 infection
Species (MHC) human (B18)
Keywords HAART, ART, acute infection
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.
- None of the 8 study subjects recognized this epitope but none were HLA B18+

HXB2 Location Nef (135–143)
Author Location p17
Epitope YPLTFGWCF
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type Intracellular cytokine staining
Keywords immunodominance, genital and mucosal immunity
References Kaul *et al.* 2003

- Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher.
- The immunodominant response was to this epitope in the PBMC of 1/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).

HXB2 Location Nef (135–143)
Author Location Nef (135–143 LAI)
Epitope YPLTFGWCY
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (B*0702)
Keywords epitope processing
References Lucchiari-Hartz *et al.* 2000

- Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152.
- All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments.
- YPLTFGWCY is the naturally processed ligand for B7, and this epitope is the only one of the five that may require trimming at the N-termini.
- YPLTFGWCY is present in low copy number in the cell, possibly due to a predominant proteasomal cleavage site between Y and P.

HXB2 Location Nef (135–143)
Author Location Nef (135–143 LAI)
Epitope YPLTFGWCY
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B*1801)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is a B*1801 epitope.

HXB2 Location Nef (135–143)
Author Location Nef (135–143)
Epitope YPLTFGWCF
Immunogen
Species (MHC) human (B*53)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (135–143)
Author Location Nef (135–143)
Epitope YPLTFGWCY
Immunogen
Species (MHC) human (B*5301)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (135–143)
Author Location
Epitope YPLTFGWCY
Epitope name Nef-YY9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*5301, B35)
Donor MHC A*3002 A*3201 B*4501 B*5301 Cw*0401 Cw*1202
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes HIGPGRAFY, gp160(310-318), HLA A*3002; AETFYVDGA, RT(437-445), HLA B*4501; and RSLYNTVATLY, p17(76-86), HLA A*3002.
- Among HIV+ individuals who carried HLA B53, 8/15 (53%) recognized this epitope – one subject also carried B7, previously shown to restrict this epitope.
- Among HIV+ individuals who carried HLA B35, 13/19 (68%) recognized this epitope.

HXB2 Location Nef (135–143)
Author Location Nef (subtype D)
Epitope YPLTFGWCF
Subtype D
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B18)
References Kaul *et al.* 2000

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.
- Low risk individuals did not have such CD8+ cells.
- CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNTVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.

HXB2 Location Nef (135–143)
Author Location Nef (135–143 LAI)
Epitope YPLTFGWCY
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B18)
References Culmann *et al.* 1991; Culmann-Penciolelli *et al.* 1994

- Nef CTL clones from HIV+ donors.

HXB2 Location Nef (135–143)
Author Location Nef (135–143 SF2)
Epitope YPLTFGWCY
Immunogen HIV-1 infection
Species (MHC) human (B18)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.

- Number of HLA-B18+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 1/2 group 2, and 0/0 group 3.

HXB2 Location Nef (135–143)
Author Location Nef
Epitope YPLTFGWCF
Immunogen HIV-1 infection
Species (MHC) human (B18)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2002

- Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.
- Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.

HXB2 Location Nef (135–143)
Author Location Nef
Epitope YPLTFGWCY
Epitope name B18-YY9(Nef)
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B18)
Donor MHC A30, A32, B18, B27
Keywords HAART, ART, supervised treatment interruptions (STI)
References Altfeld *et al.* 2002b

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).

HXB2 Location Nef (135–143)
Author Location (C consensus)
Epitope YPLTFGWCF
Subtype C
Immunogen HIV-1 infection
Species (MHC) human (B18, B*5301)
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords cross-presentation by different HLA, characterizing CD8+ T cell responses
References Kiepiela *et al.* 2004

- HLA class I restricted CD8+ T-cell responses against HIV-1 were analysed in African patients. Significantly greater number of responses were shown to be HLA-B restricted. Viral load, CD4 count and so the rate of disease progression were also associated with HLA-B alleles. In addition, the selection pressure imposed on HIV-1 by HLA-B alleles was shown to be substantially greater than by other alleles.
- This eptiope was suggested to be the epitope within a longer reactive peptide based on correspondence with a known epitope in the HIV database. Also, a significantly higher frequency of people in the Durban cohort who reacted with the peptide had this HLA type.

HXB2 Location Nef (135–143)
Author Location Nef (135–143)
Epitope YPLTFGWCY
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (B18, B49)
Keywords HIV exposed persistently seronegative (HEPS), immunodominance
References Kaul *et al.* 2001a

- Variants YPLTFGWC(Y/F) are specific for the B/D clades.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.
- Among HLA-B18 women, 1/4 HEPS and 8/9 HIV-1 infected women recognized this epitope, likelihood ratio 5.3, p value 0.04, and HEPS women tended to respond to FRDYV-DRF(Y/F)K, while infected women tended to respond to YPLT-FGWC(Y/F)
- The dominant response to this HLA allele was to this epitope for the one reactive HEPS case and in all 8/9 HIV-1 infected women.
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.

HXB2 Location Nef (135–143)
Author Location Nef (139–147 SF2)

Epitope YPLTFGWCF
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Shiga *et al.* 1996

- Binds HLA-B*3501.

HXB2 Location Nef (135–143)
Author Location Nef (135–143 BRU)
Epitope YPLTFGWCY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- YPLTFGWCY was recognized in 2/13 (15%) of individuals with HLA B7, and 11/14 (79%) of individuals with HLA B35, and it was a moderate affinity HLA binder.

HXB2 Location Nef (135–143)
Author Location Nef
Epitope YPLTFGWCY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
Donor MHC A3, A11, B35, B51
Keywords mother-to-infant transmission
References Sabbaj *et al.* 2002a

- IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release.
- T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known B35 epitope YPLTFGWCY.
- The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.

HXB2 Location Nef (135–143)
Author Location Nef
Epitope YPLTFGWCY
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B49)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A subtype consensus is identical to the B clade epitope.
- The D subtype consensus is ypltfgwcF.

HXB2 Location Nef (135–143)
Author Location Nef (subtype B)
Epitope YLPTFGWCY
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (B49)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among A and B clade viruses.
- The Clade D version of the epitope, YPLTFGWCF, was preferentially recognized by CTL.

HXB2 Location Nef (135–143)
Author Location
Epitope YPLTFGWCY
Immunogen HIV-1 infection
Species (MHC) human (B49)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope, YPLTFGWC(Y/F), was recognized in 1/22 HEPS sex worker controls (ML1668)

HXB2 Location Nef (135–143)
Author Location Nef (135–143 BRU)
Epitope YPLTFGWCY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B7)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- YPLTFGWCY was recognized in 2/13 (15%) of individuals with HLA B7, and 11/14 (79%) of individuals with HLA B35, and it was a moderate affinity HLA binder.

HXB2 Location Nef (135–143)
Author Location Nef (135–143)
Epitope YPLTFGWCY
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B7 supertype)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the most frequently recognized of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location Nef (136–144)
Author Location Nef (136–144 BRU)
Epitope PLTFGWCYK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- PLTFGWCYK was recognized in 3/12 (25%) of individuals with HLA A3. It was a low affinity HLA-A3 binder.

HXB2 Location Nef (136–145)
Author Location Nef (136–145)
Epitope PLTFGWCYKL
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords binding affinity, dendritic cells, Th1
References Wilson *et al.* 1999b

- Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors.
- Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within.
- B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL.
- Noted in Brander *et al.*, 1999 this database, to be A*0201.

HXB2 Location Nef (136–145)
Author Location Nef (136–145 LAI)
Epitope PLTFGWCYKL
Subtype B
Immunogen
Species (MHC) human (A*0201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0201 epitope.

HXB2 Location Nef (136–145)
Author Location Nef (136–145 LAI)
Epitope PLTFGWCYKL
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords epitope processing
References Lucchiari-Hartz *et al.* 2000

- Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152.
- All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments.
- The CTL that recognized PLTFGWCYKL also recognized PLTFGWCYKLV, and both forms of the epitope are naturally processed and both seem to be the direct product of a proteasomal digest, although in low copy number.

HXB2 Location Nef (136–145)
Author Location Nef (136–145)
Epitope PLTFGWCYKL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- Three of seven patients responded to this peptide with GzB producing cells and three of the patients responded with IFN-gamma producing cells. Only one patient had both a GzB and IFN-gamma response.

HXB2 Location Nef (136–145)
Author Location Nef (136–145)
Epitope PLTFGWCFKL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Durali *et al.* 1998

- Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia.
- Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested.
- Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag.
- Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef.
- Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env.
- Patient B18 had the greatest breadth and diversity of response, and recognized Gag SLYNTVATL and Nef PLTFGWCFKL.

HXB2 Location Nef (136–145)
Author Location Nef (157–166)
Epitope PLTFGWCFKL
Immunogen Vaccine
Vector/Type: DNA prime with vaccinia boost
Species (MHC) human (A2)
References Woodberry *et al.* 1999

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice.
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- PLTFGWCFKL was recognized by 1 of the HLA-A2 patients.

HXB2 Location Nef (136–145)
Author Location Nef (135–144 93TH253 subtype CRF01)
Epitope PLTFGWCYKL
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 0/4 tested FSWs recognized the E clade version of this epitope PLCFGWCFKL, which differs from the previously defined B clade version by two amino acids, PLTFGWCYKL.
- This epitope was only conserved in CRF01 (subtype E) and subtype B.

HXB2 Location Nef (136–145)
Author Location Nef (136–145)
Epitope PLTFGWCYKL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

HXB2 Location Nef (136–145)
Author Location
Epitope PLTFGWCYKL
Epitope name Nef-PL10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
References Sabbaj *et al.* 2002b

- Among HIV+ individuals who carried HLA A02, 3/29 (10%) recognized this epitope.

HXB2 Location Nef (136–145)
Author Location Nef (136–145 BRU)
Epitope PLTFGWCYKL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords binding affinity, epitope processing
References Choppin *et al.* 2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- PLTFGWCYKL was recognized in 9/28 (32%) of individuals with HLA A2. It was a low affinity HLA-A2 binder.

HXB2 Location Nef (136–145)
Author Location Nef (136–145)
Epitope PLTFGWCYKL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A2)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This was one of the most highly recognized of the 31 peptides that were shown to elicit a response.

HXB2 Location Nef (136–146)
Author Location Nef (136–146 LAI)
Epitope PLTFGWCYKLV
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords epitope processing
References Lucchiari-Hartz *et al.* 2000

- Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152.
- All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments.
- The CTL that recognized PLTFGWCYKL also recognized PLTFGWCYKLV, and both forms of the epitope are naturally processed and both seem to be the direct product of a proteasomal digest, although in low copy number.

HXB2 Location Nef (137–145)
Author Location Nef (139–147 HXB3)
Epitope LTFGWCFKL
Immunogen Vaccine
Vector/Type: DNA, peptide *Strain:* B clade HXB3 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (A*0201)
Keywords binding affinity, computational epitope prediction
References Sandberg *et al.* 2000

- Ten Nef 9-mer peptides were predicted to have a strong binding affinity with HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly.
- A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with either nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by gene gun – LTFGWCFKL did not elicit a CTL response.
- LTFGWCFKL was also tested by subcutaneous injection of Nef peptides in Freund's adjuvant, because it bound strongly to HLA-A*0201, and the peptide vaccination did elicit a response.
- The lack of response to the nef DNA vaccine and the response to the peptide suggests LTFGWCFKL may not be processed.

HXB2 Location Nef (137–145)
Author Location Nef (137–)
Epitope LTFGWCFKL
Epitope name Nef137
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This epitope was one of the previously identified HLA-A2 epitopes studied.
- 3/17 HIV-infected HLA-A2+ people recognized this epitope.

HXB2 Location Nef (137–145)
Author Location Nef (137–145)
Epitope LTFGWCYKL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A2)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This was one of the most highly recognized of the 31 peptides that were shown to elicit a response.

HXB2 Location Nef (137–145)
Author Location Nef (137–145)
Epitope LTFGWCFKL
Epitope name Nef137-145
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords responses in children, immunodominance, characterizing CD8+ T cell responses
References Chandwani *et al.* 2004

- Responses to five HLA-A2 presented epitopes in Nef were characterized in a population of 19 HIV infected adults and 21 children. The CD8 T-cell response to Nef was stronger and broader in adults than children, averaging 652 and 87 SFCs/10^6 PBMC, and 2.6 and 0.9 recognized epitopes per person, respectively.
- This epitope was second in an immunodominance hierarchy of the five A02 Nef epitopes studied.

HXB2 Location Nef (137–145)
Author Location Nef (158–166)
Epitope LTFGWCFKL
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)

HXB2 Location Nef (137–146)
Author Location Nef (221A)
Epitope LTFGWCFKLV
Epitope name Nef-221a
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- 1/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT.
- 2/12 acutely infected individuals recognized this epitope.
- LTFGWCFKLV binds to five HLA-A2 supertype alleles:A*0203, A*0201 (highest affinity), A*0206, A*6802 and A*0202.

HXB2 Location Nef (137–146)
Author Location Nef (158–167)
Epitope LTFGWCFKLV
Immunogen HIV-1 infection
Species (MHC) human (A2 supertype)
Keywords supertype, rate of progression
References Propato *et al.* 2001

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)
- Tetramer staining with A2, beta2microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific sells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population.

HXB2 Location Nef (141–148)
Author Location Nef (141–)
Epitope WCFKLVPV
Epitope name Nef141
Immunogen HIV-1 infection, Vaccine *Vector/Type:* peptide *HIV component:* Nef *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was an intermediate A2 binder, and induced a CD8+ T-cell IFN gamma response in 1/6 mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.

HXB2 Location Nef (162–181)
Author Location Nef (161–180)
Epitope TSLLHPVSLHGMDDPEREVL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1995

- HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.

HXB2 Location Nef (162–181)
Author Location Nef (161–180 SF2)
Epitope TSLLHPVSLHGMDDPEREVL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- One of these 11 had CTL response to this peptide.

HXB2 Location Nef (162–181)
Author Location Nef (101–120 SF2)
Epitope TSLLHPVSLHGMDDPEREVL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997b

- CTL expanded *ex vivo* were later infused into HIV-1 infected patients.

HXB2 Location Nef (162–181)
Author Location Nef (161–180 SF2)
Epitope TSLLHPVSLHGMDDPEREVL
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- One of these 11 had CTL response to this peptide.

HXB2 Location Nef (166–177)
Author Location Nef (160–179 SF2)
Epitope HPVSLHGMDDPE
Immunogen HIV-1 infection
Species (MHC) human (B35)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3.

HXB2 Location Nef (172–191)
Author Location Nef (171–190 SF2)
Epitope GMDDPEREVLEWRFDSRLAF
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-A2, B21.

HXB2 Location Nef (175–184)
Author Location Nef (175–184)
Epitope DPEKEVLQWK
Immunogen HIV-1 infection
Species (MHC) human (B7)
References Jin *et al.* 2000b

- This a B7 epitope, a subdominant CTL response, was defined by an un-conventional approach used to predict epitopes in an HLA B7+ long-term non-progressor.
- Three additional sub-dominant HLA B7 epitopes were defined using EpiMatrix, a non-anchor based strategy for defining potential epitopes, which highlighted 2078 possible epitopes in the autologous HIV-1 derived from the study subject, followed by B7 anchor residue prediction which narrowed the set to 55 peptides, three of which could serve as functional CTL epitopes.

HXB2 Location Nef (180–189)
Author Location Nef (180–189 LAI)
Epitope VLEWRFDSRL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
References Haas *et al.* 1996; Haas *et al.* 1997

- There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection.
- Noted in Brander *et al.*, 1999 this database, to be A*0201.

HXB2 Location Nef (180–189)
Author Location Nef (180–189 LAI)
Epitope VLEWRFDSRL
Subtype B
Immunogen
Species (MHC) human (A*0201)
Keywords optimal epitope
References Frahm *et al.* 2004

- C. Brander notes this is an A*0201 epitope.

HXB2 Location Nef (180–189)
Author Location Nef (180–189 LAI)
Epitope VLMWQFDSRL
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* natural variants *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) transgenic mouse (A*0201)
Keywords binding affinity, vaccine-specific epitope characteristics
References Boissonnas *et al.* 2002

- Ten naturally occurring variants of this epitope were tested for their affinity to HLA-A*0201 and for their ability to induce gamma-IFN and cytotoxic functions through vaccination of HLA-A*0201 transgenic mice.
- Only two variants could induce vaccine responses: VLMWQFDSRL, a high affinity binder, and VLQWRFDSRL a medium affinity binder to A*0201.
- In vivo priming with Nef peptide VLMWQFDSRL induced cross-reactive CTL to 6/7 peptides tested (AlmwKfdsKl, vlmwKfdsrl, vlmwKfdsKl, vlQwRfdsKl, vlVwrfdTrl, and vlAwKLdsrl but not the LAI peptide vlEwrfdsrl)
- In vivo priming with Nef peptide VLQWRFDTRL induced cross-reactive CTL to 3/6 variant Nef peptides (vlMwQfdsrl, vlqwrfdSrl and vlEwrfdsrl).

HXB2 Location Nef (180–189)
Author Location Nef (190–198)
Epitope VLEWRFDSRL
Immunogen Vaccine
Vector/Type: DNA *HIV component:* HIV-1
Species (MHC) mouse (A*0201)
Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance
References Singh *et al.* 2002; Sykes & Johnston 1999

- C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome.
- A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members.
- Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV (Pol), RIQRGPGRAFVTIGK (Env) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen.
- The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.

HXB2 Location Nef (180–189)
Author Location Nef (180–189)
Epitope VLEWRFDSRL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- Three of seven patients responded to this peptide with GzB producing cells, while one of the three patients responded with IFN-gamma producing cells.

HXB2 Location Nef (180–189)
Author Location Nef (180–189)
Epitope VLEWRFDSRL
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
Keywords binding affinity, dendritic cells, Th1
References Wilson *et al.* 1999b

- Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors.
- Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within.
- B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL.

HXB2 Location Nef (180–189)
Author Location Nef (180–189)
Epitope VLEWRFDSRL
Immunogen Vaccine
Vector/Type: DNA prime with vaccinia boost
Species (MHC) human (A2)
References Woodberry *et al.* 1999

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice.

- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- VLEWRFDSRL was recognized by 2 of the HLA-A2 patients.

HXB2 Location Nef (180–189)
Author Location Nef (180–189 LAI)
Epitope VLEWRFDSRL
Epitope name N3
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART
References Mollet *et al.* 2000

- A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses.
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.

HXB2 Location Nef (180–189)
Author Location Nef (179–188 93TH253 subtype CRF01)
Epitope VLEWRFDSRL
Subtype CRF01_AE
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords inter-clade comparisons
References Bond *et al.* 2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 0/4 tested FSWs recognized the E clade version of this epitope VLIWKFDSAL, which differs from the previously defined B clade version by three amino acids, VLEWRFDSRL.

HXB2 Location Nef (180–189)
Author Location Nef (180–189)
Epitope VLEWRFDSRL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords rate of progression, acute infection
References Day *et al.* 2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

HXB2 Location Nef (180–189)
Author Location Nef (178–187)
Epitope VLEWRFDSRL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- 5/19 patients recognized this epitope.

HXB2 Location Nef (181–189)
Author Location Nef (181–189)
Epitope LEWRFDSRL
Epitope name Nef181-189
Immunogen HIV-1 infection
Species (MHC) human (A2)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords responses in children, immunodominance, characterizing CD8+ T cell responses
References Chandwani *et al.* 2004

- Responses to five HLA-A2 presented epitopes in Nef were characterized in a population of 19 HIV infected adults and 21 children. The CD8 T-cell response to Nef was stronger and broader in adults than children, averaging 652 and 87 SFCs/10^6 PBMC, and 2.6 and 0.9 recognized epitopes per person, respectively.
- This was not the immunodominant response.

HXB2 Location Nef (182–189)
Author Location Nef (182–189)
Epitope EWRFDSRL
Subtype B
Immunogen Vaccine

Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (B8)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of the 31 epitopes that the vaccinated volunteers responded to.

HXB2 Location Nef (182–198)
Author Location Nef (182–198 BRU)
Epitope EWRFDSRLAFHHVAREL
Immunogen HIV-1 infection
Species (MHC) human (A1, B8)
References Hadida *et al.* 1992

- HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.

HXB2 Location Nef (182–198)
Author Location Nef (182–198 LAI)
Epitope EWRFDSRLAFHHVAREL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2, A25(10))
References Hadida *et al.* 1995

- The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions.

HXB2 Location Nef (182–198)
Author Location Nef (182–198 BRU)
Epitope EWRFDSRLAFHHVAREL
Immunogen HIV-1 infection
Species (MHC) human (A25)
References Cheynier *et al.* 1992

- CTL isolated in children born to HIV-1 positive mothers.

HXB2 Location Nef (182–198)
Author Location Nef (182–198 LAI)
Epitope EWRFDSRLAFHHVAREL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Hadida *et al.* 1995

- The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions.

HXB2 Location Nef (182–198)
Author Location Nef (182–198 LAI)
Epitope EWRFDSRLAFHHVAREL
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia, Mengo virus *Strain:* B clade LAI *HIV component:* Nef
Species (MHC) mouse (H-2^d)
References Van der Ryst *et al.* 1998

- Macaca mulatta did not have a detectable response to Rec Mengo virus-HIV-1 Nef 65-206 vaccine.
- BALB/c mice had a weak response to this epitope in the Mengo virus construct – in contrast, HIV-1 Nef induces a strong CTL response in mice when presented in a vaccinia background.

HXB2 Location Nef (182–201)
Author Location Nef (191–205 SF2)
Epitope EWRFDSRLAFHHVARELHPE
Immunogen HIV-1 infection
Species (MHC) human
References Lieberman *et al.* 1997a

- Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.
- Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.
- One of these 11 had CTL response to this peptide.
- The responding subject was HLA-A2, B21.

HXB2 Location Nef (182–205)
Author Location Nef (182–205 LAI)
Epitope EWRFDSRLAFHHVARELHPEYFKN
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 4/10 reacted to this Nef peptide.
- 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual.
- None of the 12 tested had an IgG response to this peptide.

HXB2 Location Nef (183–191)
Author Location
Epitope WRFDSRLAF
Epitope name Nef-WF9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Donor MHC A*2904 A*3002 B*1503 B*5802 Cw*0202 Cw*0602
Keywords HAART, ART
References Sabbaj *et al.* 2002b

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.

- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- This epitope was newly defined in this study.
- Subject 01RCH50 also recognized the epitope RMRGAHT-NDV, RT(356-365), A*3002 – she was African American, was on HAART, had a viral load of 960 and CD4 count of 728.
- Among HIV+ individuals who carried HLA B15, 3/17 (18%) recognized this epitope.

HXB2 Location Nef (183–191)
Author Location Nef (183–191)
Epitope WRFDSRLAF
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Keywords optimal epitope
References Frahm *et al.* 2004

HXB2 Location Nef (183–191)
Author Location Nef (183–191)
Epitope WRFDSRLAF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*1503)
Donor MHC A*2301, B*3501, B*1503 (B72), Cw2, Cw7
Assay type CD8 T-cell Elispot - IFNγ
Keywords binding affinity, acute infection, early-expressed proteins
References Cao *et al.* 2003

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

HXB2 Location Nef (186–193)
Author Location Nef (186–193 LAI)
Epitope DSRLAFHH
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35)
References Hadida *et al.* 1995

- The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions.

HXB2 Location Nef (186–194)
Author Location Nef (186–194)
Epitope DSRLAFHHM
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A24)
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location Nef (186–194)
Author Location Nef (186–194)
Epitope DSRLAFHHM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A24)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- Two of seven patients responded to this peptide with GzB producing cells, while none of the patients responded with IFN-gamma producing cells.

HXB2 Location Nef (186–194)
Author Location Nef (186–194 BRU)
Epitope DSRLAFHHV
Immunogen
Species (MHC) human (B51)
References Connan *et al.* 1994

- Resulted in the assembly of HLA-B51.

HXB2 Location Nef (186–194)
Author Location Nef (186–194)
Epitope DSRLAFHHV
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 7 epitopes from this individual that varied over time, although the internal mutations did not become fixed.The dsLlaLRhM variant residues arose at early time points, and the dsrlaVhhv variant residue arose at intermediate time points.

HXB2 Location Nef (188–196)
Author Location Nef (192–200 SF2)
Epitope KLAFHHMAR
Subtype B
Immunogen HIV-1 infection, computer prediction
Species (MHC) human (A*3303)
Assay type Chromium-release assay
Keywords binding affinity, computational epitope prediction
References Hossain *et al.* 2003

- HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individuals, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing.
- This epitope is one of the 2/6 peptides that could induce CTL responses in the PBMC of infected individuals, but was not properly processed in a vaccinia-HIV infected target cell.

HXB2 Location Nef (188–196)
Author Location Nef (188–196 LAI)
Epitope RLAFHHVAR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B52)
References Hadida *et al.* 1995

- The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions.

HXB2 Location Nef (188–201)
Author Location Nef (188–201 LAI)
Epitope RLAFHHVARELHPE
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B35, Cw4)
References Buseyne *et al.* 1993a

- Vertical transmission of HIV ranges from 13% to 39%
- Primary assays showed that cytotoxic activity against at least one HIV protein was detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study.

HXB2 Location Nef (190–198)
Author Location
Epitope ALKHRAYEL
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001c

- This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.
- The epidemiological factor associated with seroconversion was stopping sex work. HIV-specific CTL activity declined when HEPS sex workers stopped working for a period or retired.
- This epitope was in 1/22 HEPS controls, ML1749.

HXB2 Location Nef (190–198)
Author Location Nef
Epitope AFHHVAREL
Epitope name Nef AL9
Immunogen HIV-1 infection
Species (MHC) human (A*0201)
Keywords inter-clade comparisons, supertype, computational epitope prediction
References Altfeld *et al.* 2001c

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, including Nef AL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- RT VL9 was not recognized by any of the 22 HLA-A2 patients with chronic HIV-1 infection or the 13 HLA-A2 patients with acute HIV-1 infection included in this study.

HXB2 Location Nef (190–198)
Author Location Nef
Epitope ALKHRAYEL
Subtype A
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade
HIV component: p17 Gag, p24 Gag
Species (MHC) human, macaque (A*0201)
Keywords inter-clade comparisons, epitope processing, immunodominance
References Hanke & McMichael 2000; Wee *et al.* 2002

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used

in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string Hanke & McMichael [2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string Wee *et al.* [2002].

HXB2 Location Nef (190–198)
Author Location Nef (190–198 LAI)
Epitope AFHHVAREL
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2)
Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Rowland-Jones *et al.* 1998a
- CTL recognition reported in the context of HLA-B52 and A2.1, A2.2 and A2.4.
- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating.
- The A subtype consensus is ALKHRAYEL.
- The D subtype consensus is AfEHKAREm.
- Hunziker *et al.* [1998] suggests that HLA-A2 does not in fact present this epitope, and notes that it does not promote A2 assembly Connan *et al.* [1994] – also see Brander *et al.* [1998b]
- Hunziker *et al.* [1998] maintains that HLA-A2 does not present this epitope contrary to an earlier report Hadida *et al.* [1995], (also see Brander *et al.* [1998a])—despite the position of Hunziker *et al.*, Rowland-Jones and colleagues are confident that this epitope in its A clade form is presented by HLA-A*0201 and A*0202, and it is one of the most common responses seen in both seropositive and exposed-uninfected donors from Nairobi (Rupert Kaul, pers. comm.)

HXB2 Location Nef (190–198)
Author Location Nef (190–198)
Epitope AFHHVAREL
Immunogen in vitro stimulation or selection
Species (MHC) human (A2)
Keywords binding affinity, dendritic cells, Th1
References Wilson *et al.* 1999b
- Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors.
- Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within.
- B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL.

HXB2 Location Nef (190–198)
Author Location Nef (190–198)
Epitope AFHHVAREL
Immunogen Vaccine
Vector/Type: vaccinia
Species (MHC) human (A2)
References Woodberry *et al.* 1999
- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice.
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- AFHHVAREL was recognized by 2 of the patients.

HXB2 Location Nef (190–198)
Author Location Nef (190–198 SF2)
Epitope AFHHVAREL
Immunogen HIV-1 infection
Species (MHC) human (A2)
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b
- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 0/10 group 1, 1/6 group 2, and 0/4 group 3.

HXB2 Location Nef (190–198)
Author Location Nef (190–198)
Epitope ALKHRAYEL
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human (A2)

Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS)
References Kaul *et al.* 2001a

- Variants ALKHRAYEL and AFHHVAREL are A/B clade specific.
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.

HXB2 Location Nef (190–198)
Author Location Nef (190–)
Epitope AFHHVAREL
Epitope name Nef190
Immunogen HIV-1 infection
Species (MHC) human (A2)
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords binding affinity, inter-clade comparisons, computational epitope prediction
References Corbet *et al.* 2003

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This epitope was one of the previously identified HLA-A2 epitopes studied.
- None of the 17 HIV-infected HLA-A2+ people in this study recognized this epitope.

HXB2 Location Nef (190–198)
Author Location Nef (190–198)
Epitope ALHHVAREL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A2)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of 31 that the vaccinated volunteers responded to.

HXB2 Location Nef (190–198)
Author Location Nef (subtype B)
Epitope AFHHVAREL
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human (A2, A*0202, A*0201)
Keywords inter-clade comparisons
References Rowland-Jones *et al.* 1998b

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- Clade A version of the epitope: ALKHRAYEL, Clade D epitope: AFEHKAREM.
- This epitope was recognized by two different exposed and uninfected prostitutes.

HXB2 Location Nef (190–198)
Author Location Nef (190–198)
Epitope AFHHVAREL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A2, B52)
Country United States.
Assay type CD8 T-cell Elispot - IFNγ, CD8 T-cell Elispot granzyme B
Keywords Th1, characterizing CD8+ T cell responses
References Kleen *et al.* 2004

- Only 20% of CD8+ T-cells produce IFN-gamma and granzyme B simultaneously (Tc1a). Two additional subpopulations of HIV specific CD8 cells are found, each one constituting 30-40% of the CD8 cell pool. One of these (Tc1b) secretes IFN-gamma only, and the other one (Tc1c) secretes GzB only.
- Three of seven patients responded to this peptide with GzB producing cells, while one of three patients also responded with IFN-gamma producing cells.

HXB2 Location Nef (190–198)
Author Location Nef (190–198 LAI)
Epitope AFHHVAREK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (A3)
References Hadida *et al.* 1995

- Naturally occurring L to K anchor substitution abrogates A2 binding, but permits HLA-A3 binding.

HXB2 Location Nef (190–198)
Author Location Nef (190–198)
Epitope AFHHVAREK
Immunogen HIV-1 infection
Species (MHC) human (A3)
Country Spain.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords HAART, ART, supervised treatment interruptions (STI), immune dysfunction
References Plana *et al.* 2004

- Structured treatment interruption (STI) alone is not able to control viral replication in chronically infected patients, probably due to lack of strong, maintained T-helper cell responses. HIV-1 specific CD8+ T-cell responses were shown to increase significantly until the end of the follow up, but were not correlated with viral load.
- Less than 2 of 14 patients recognized this epitope.

HXB2 Location Nef (190–198)
Author Location Nef (190–198)
Epitope AFHHVAREK
Immunogen HIV-1 infection
Species (MHC) human (B51)
Donor MHC A03, A32, B51, B15, Cw03, Cw06, DR4, DR8, DQ7
Country Netherlands.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords rate of progression, escape
References Geels *et al.* 2003

- Both stable potential epitopes and epitopes with escape mutations were found in a patient with increasing viral load over a time period of 4 years. Fixation of escape mutations occured sequentially and correlated with the rise in viral load and with the increased number of productively infected cells.
- This is one of 7 epitopes from this individual that varied over time, although the internal mutations did not become fixed. The aLRhMarek variant residues arose at early time points, the aVhhvarek variant residue arose at intermediate time points, and afhhvaXeI variant residues arose at late time points.

HXB2 Location Nef (192–206)
Author Location Nef (192–206 BRU)
Epitope HHVARELHPEYFKNC
Immunogen HIV-1 infection
Species (MHC) human (A1)
References Hadida *et al.* 1992

- HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.

HXB2 Location Nef (195–202)
Author Location Nef (195–202)
Epitope ARELHPEY
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Env, Gag, Nef *Adjuvant:* QS21
Species (MHC) human (A1)
Assay type proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization
References Gahéry-Ségard *et al.* 2003

- After injection of an anti-HIV-1 lipopeptide vaccine and the booster injections, a response was observed in >85% of 28 volunteers, and a long-term immune response was observed in >50% of the volunteers. A positive effect of QS21 adjuvant was found for B-and CD4+T-cell responses. A higher number of CD8+ T-cell epitopes was induced after a fourth boost injection. This epitope was one of 31 that were recognized in the vaccinees.

HXB2 Location Nef
Author Location Nef (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1
References Wasik *et al.* 2000

- HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of beta-chemokines and IL-2 relative to other HIV+ infants.
- No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors.
- CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References De Maria *et al.* 1997

- CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function.
- Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Lubaki *et al.* 1999

- Three strategies were used to analyze CTL activity: area under the net HIV-specific lysis curve (ACU), linear regression (LR) of net specific lysis, and the standard method, lytic units (LU20)
- A correlation between low HIV plasma viral load and increased levels of HIV-specific Gag and Nef CTL activity was observed using ACU and LR, but not LU20.

HXB2 Location Nef
Author Location Nef (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade LAI, B clade SF2 *HIV component:* Env, Gag, Nef, Protease
Species (MHC) human
References Gorse *et al.* 1999b

- The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120.

- In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients.
- The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords TCR usage
References Gamberg *et al.* 1999

- 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL *in vitro*, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens.
- Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR betaV gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat
Species (MHC) human
Keywords HAART, ART
References Calarota *et al.* 1999

- 9/9 HIV-1 + subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated.
- The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses.
- Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.

HXB2 Location Nef
Author Location Nef (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Buseyne *et al.* 1998a

- This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load.

HXB2 Location Nef
Author Location Nef (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Buseyne *et al.* 1998b

- In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes.

HXB2 Location Nef
Author Location Nef (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: canarypox *HIV component:* Gag, gp120, gp41, Nef, Protease, RT
Species (MHC) human
References Evans *et al.* 1999

- A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References da Silva & Hughes 1998

- CTL dense regions of Nef tend to lie in conserved domains with low non-synonymous substitution per site – authors consider that this may be due to a host adaptation to infection that focuses the CTL response to be directed against conserved functional domains da Silva & Hughes [1998]

HXB2 Location Nef
Author Location Nef (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Legrand *et al.* 1997

- Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat.
- An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef.
- Early responses to Pol, Rev, Vif and Tat were rare.

HXB2 Location Nef
Author Location Nef (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Zerhouni *et al.* 1997

- CTL responses to Env, Gag, Nef and RT were tested at various phases of disease progression – 10 asymptomatic patients generally had CTL responses to all proteins, 10 ARC patients responded well to all proteins except Nef, and AIDS patients had few responses to any proteins.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC)
Keywords epitope processing
References Kuiken *et al.* 1999

- A correlation between conserved regions of Nef and CTL epitope density was also noted in Kuiken *et al.* [1999]. The authors suggest that this may be due to biological reasons such as the one described above da Silva & Hughes [1998], or due to epitope processing, or may possibly be an artifact of experimental strategy for epitope definition such that conserved epitopes would tend to be identified because they would be more likely to be cross-reactive with the test reagents.
- Both p17 and Nef show a correlation between epitope density and conserved regions in the protein – in contrast, p24 is a more conserved protein and known epitopes are evenly distributed across p24.

HXB2 Location Nef
Author Location Nef (BRU)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Aladdin *et al.* 1999

- In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death.

HXB2 Location Nef
Author Location Nef (SF2)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Jin *et al.* 1998a

- CTL precursor frequencies were determined in HIV-1 infected pregnant women, and higher CTLp frequencies to Pol and SF2 Nef, but not IIIB Nef, were found in non-transmitting mothers than in transmitting mothers – Nef CTL responses have been found in uninfected infants born to HIV+ women (Lazuriaga95);

HXB2 Location Nef
Author Location (subtype C)
Epitope
Subtype C
Immunogen
Species (MHC) human
Keywords inter-clade comparisons, immunodominance
References Novitsky *et al.* 2001

- This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort.
- 37 of 45 subjects (82%) demonstrated Nef specific ELISPOT CTL responses of more than 100 SFC/106 PBMC.
- Two Nef-immunodominant regions were identified, one spanned amino acid positions 67 to 96 using HXB2 numbering system while the second corresponded to amino acid positions 122 to 141.
- While there was some subtype B and C cross-reactivity, there was greater breadth and intensity of response if the CTL from HIV-1-infected individuals was probed with ELISPOT using peptides derived from the same subtype (a median of three Nef epitopes recognized within subtype C compared with one Nef epitope recognized from subtype B peptides, and ELISPOT results with a median of 763 SFC/106 PBMC among responses to HIV-1 C, versus a median of 318 SFC/106 PBMC among responses to HIV-1 B.

HXB2 Location Nef
Author Location Nef (subtype A, B, D)
Epitope
Subtype A, B, D
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons
References Cao *et al.* 2000

- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D.
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS)
Species (MHC) human
Keywords review
References Calarota & Wahren 2001

- This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asymptomatic HIV+ individuals.

HXB2 Location Nef
Author Location
Epitope
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References De Maria *et al.* 1994; Kuhn *et al.* 2002

- 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location Nef
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, escape
References Yusim *et al.* 2002

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.
- In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.

HXB2 Location Nef
Author Location Nef (HXB)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords epitope processing, vaccine-specific epitope characteristics
References Lu *et al.* 2000a

- Bacillus anthrax lethal toxin (LFn)-HIV fusion proteins are candidate HIV vaccines that are safe in mice, and LFn-V3 region fusion proteins induce CD8 T cells in BALBc mice. LFn causes exogenous protein to be taken up and processed in a class I pathway. Expressed proteins from Gag p24 and nef fragments cloned into the LFn expression plasmid stimulate gag-specific CD4 proliferation and CTL responses in HIV-infected donor PBMCs *in vitro*.

HXB2 Location Nef
Author Location (BRU)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Edwards *et al.* 2002

- 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag.
- Nef and/or Pol CTL responses were detected in 86% of the subjects.
- The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load.
- Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count.
- Nef and Env responses did not correlate with either CD4 counts or viral load.

HXB2 Location Nef
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, dendritic cells
References Larsson *et al.* 2002b

- Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.

HXB2 Location Nef
Author Location (SF2)
Epitope
Subtype B
Immunogen HIV-1 and HCV co-infection
Species (MHC) human
Keywords rate of progression
References Lauer *et al.* 2002

- HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins.
- All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load.
- Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted.
- HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.

HXB2 Location Nef
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, responses in children
References Scott *et al.* 2001

- CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age.

- Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses.
- One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol.
- Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.

HXB2 Location Nef
Author Location (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, supervised treatment interruptions (STI)
References Ortiz *et al.* 2001

- Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.

HXB2 Location Nef
Author Location
Epitope
Immunogen Vaccine
Vector/Type: adenovirus *HIV component:* Gag-Pol, Nef, Vpr
Species (MHC) mouse
References Muthumani *et al.* 2002

- Vpr can cause cells to go into G2 arrest, and it surpresses immune cell activation and inflammatory cytokine production, so co-immunization of BALB/c mice with recombinant adenovirus expressing Vpr and HIV-1 antigens Nef or Gag/Pol was tested to see if Vpr reduced the immune response to the other HIV antigens.
- Vpr compromised CD8+ T-cell lytic responses and T-helper proliferative responses in mice co-immunized with Vpr and Nef or Gag/Pol.
- In vitro, Vpr reduced T-cell cytokine production of IL-12 and TNFalpha, indicative of Vpr-mediated immune suppression.

HXB2 Location Nef
Author Location Nef
Epitope
Subtype multiple
Immunogen
Species (MHC) human
Assay type Flow cytometric CTL assay
Keywords inter-clade comparisons
References Currier *et al.* 2003

- CD8-cellular immune responses from 21 HIV-1 infected patients from Kenya infected with subtype A, C, D, and unique recombinants were studied for cross-recognition of Gag, Env, and Nef vaccinia-expressed proteins representing subtypes A-H, including CRF01.
- Both subtype-specific and cross-reactive CTL were observed, with a skewing of responses towards the infecting subtype in the nine subjects with full length sequence available. The magnitude of the responses to Gag were the highest, less to Nef, and still less to Env.
- For Gag, 8/21 subjects responded to at least 7/8 different subtype proteins, 7 had a mixed response, recognizing some subtypes but not others, and 6 responded to only one or none of the different subtype proteins. For Env, 4/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 7 responded to one or none. For Nef, 5/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 6 responded to one or none.

HXB2 Location Nef
Author Location Nef (B.AU.AF064676)
Epitope
Subtype B
Immunogen
Species (MHC) human
References

HXB2 Location Nef
Author Location Nef
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords assay standardization/improvement
References Draenert *et al.* 2003

- Six different HIV-1 Nef peptide sets ranging in length from 15-20 amino acids with overlap from 10-11 amino acids derived from either the B clade consensus sequences or the B clade sequence B.AU.AF064676 were used to study the impact of using different peptide design strategies to detect CD4 and CD8 T-cell responses. 20 individuals were tested using the six sets of peptides. 17/20 had CD8 T-cell responses to all peptides sets, and 15 of these 17 had CD4 T-cell responses.
- Although there was a trend in detecting more CD8 T cell responses using the shorter 15-mer peptides, longer 20-mers were best for detecting more CD4 T-cell responses, but neither result was statistically significant. Similar results were seen in the 15 to 20 amino acid range for both IFN gamma Elispot and ICS assays.
- Use of the consensus versus the natural strain identified slightly increased numbers of reactive peptides. Seven reactive peptides were observed with the B consensus peptides but not the B.AU.AF064676 peptides, but on the other hand four reactivites were observed using the B.AU.AF064676 peptides but not the consensus.
- Using an overlap of 10 or 11 amino acids did not make a difference.

HXB2 Location Nef
Author Location (C consensus)
Epitope
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ
Keywords rate of progression
References Novitsky *et al.* 2003

- In this study, PBMC from 105 asymptomatic HIV-1 C clade infected patients from Botswana were screened for HIV-1 subtype C specific T-cell responses directed against Gag, Pol, Vif, Vpr, Tat, Rev, Vpu, Env and Nef. Nef-specific T-cell responses positively correlated with plasma viral load. In contrast, HIV-1 Gag and especially Gag p24 showed an inverse correlation with viral load.

HXB2 Location Nef
Author Location (C consensus)
Epitope
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ
Keywords rate of progression
References Novitsky *et al.* 2003

- In this study, PBMC from 105 asymptomatic HIV-1 C clade infected patients from Botswana were screened for HIV-1 subtype C specific T-cell responses directed against Gag, Pol, Vif, Vpr, Tat, Rev, Vpu, Env and Nef. Nef-specific T-cell responses positively correlated with plasma viral load. In contrast, HIV-1 Gag and especially Gag p24 showed an inverse correlation with viral load.

HXB2 Location Nef
Author Location Nef
Epitope
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Country South Africa.
Assay type CD8 T-cell Elispot - IFNγ
Keywords rate of progression, immunodominance, acute infection, early-expressed proteins
References Masemola *et al.* 2004a

- Anti-HIV T-cell responses in subtype C HIV-1 infected individuals in the beginning of the infection target multiple protein regions, but the responses are dominated by Nef, making up almost one-third of the total responses. 97.5% of the Nef epitopes targeted were within a short stretch of 119 amino acids.
- Neither breadth nor magnitude of CD8+ T-cell responses were correlated with control of virus, however hierarchical preferential targeting of Gag was significantly associated with lower viral loads.

HXB2 Location Nef
Author Location Nef (B consensus)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords HAART, ART, immunodominance, acute infection, vaccine antigen design
References Lichterfeld *et al.* 2004b

- HIV-1 specific CD8 T-cell responses in individuals with acute and early HIV-1 infection are preferentially directed against epitopes in the central region of Nef, with 94% of the magnitude of the response in acute infection directed at Nef, and 46% during early infection. In chronic infection, CD8 T-cell immune responses are broadly diversified towards Gag, Env and Pol, and Nef accounts for only 17% of the response.
- The region of Nef that is targeted is the central most conserved region, but relative to other HIV proteins it is still quite variable. However, responses are cross-reactive enough to detect strong acute responses using consensus based peptides, and is an early expressed gene so may have advantages in the context of a vaccine.
- Nef immunodominance was retained in patients that were treated during acute infection, but no treatment and so continuous antigen exposure resulted in rapid diversification of the immune response.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC) human (A*0201, Cw*08)
References Shacklett *et al.* 2000

- HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples.

HXB2 Location Nef
Author Location Nef
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (B*35)
Keywords rate of progression
References Jin *et al.* 2002

- Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501.
- Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env.
- The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.

HXB2 Location Nef
Author Location Nef
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Bupivacaine
Species (MHC) mouse (H-2^d)
Assay type CD8 T-cell Elispot - IFNγ
Keywords class I down-regulation by Nef, vaccine antigen design
References Majumder *et al.* 2003

- Non-functional Nef vaccine constructs that do not down-regulate class I or CD4 proteins are shown to be capable of inducing primary and memory T cell immune response after DNA vaccination in BALB/c mice, which makes them good candidates for vaccines.
- The responses to peptide pools suggest the C-terminal region of Nef is more immunogenic (the two most reactive peptide pools spanned positions 126-175, and positions 166-215).

HXB2 Location Nef
Author Location Nef (BRU)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade BRU *HIV component:* Nef
Species (MHC) mouse (H-$2D^d$)
References Collings *et al.* 1999

- A comparison of DNA vaccination with HIV-1 Nef expression vectors pBN-CMV-NEF and pBN-RSV-NEF (self-replicating), pCGE2-NEF (non-replicating).
- CTL immune responses were detected using all three expression vectors, while a humoral immune response to Nef was only observed in the self-replicating expression vectors; possibly antibody responses require higher levels of protein expression.

HXB2 Location Nef
Author Location Nef (SIV)
Epitope
Immunogen SIV infection
Species (MHC) macaque (Mamu-A*11, -B*03, -B*04, -B*17)
References Dzuris *et al.* 2000

- Cell binding assays for Mamu molecules were employed to describe the peptide binding motifs for Mamu-A*11, -B*03, -B*03, -B*04, and -B*17 CTL epitopes – a similarity for Mamu-A*11 and -B*03 and human HLA-B*44 and -B*27, respectively, was observed – all epitopes studied were SIV epitopes, so not specifically listed here.

II-B-22 HIV-1 CTL, CD8+, epitopes

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Schito *et al.* 2001

- Longitudinal analysis (72 weeks) of 15 patients with acute or recent HIV-1 infection implies that HAART treatment alone can not completely conserve CD8+ cell homeostasis and preserve the original T-cell receptor repertoire.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Mackewicz *et al.* 2000

- Non-cytotoxic anti-HIV responses of CD8+ T cells cultured with CD4 infected HIV cells are mediated be blocking expression of viral RNA, and do not influence viral replication steps through integration of provirus.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC)
Keywords dynamics
References Altes *et al.* 2002

- This study employs a mathematical model to study the consequences of increasing the T-helper response through a vaccine, which would have counter-balancing effects in a new infection: a more intense response provides more help but also more target cells. The model indicates that if the infecting virus had a low replication rate, then CTLp and CD4 helper cells could control an infection. Only a vaccine that could increase CTL responsiveness could reduce viral set point with observed replication rates.
- A CD4+ T-cell response without maintained CTL response was deleterious in this model.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords assay standardization/improvement
References Currier *et al.* 2002b

- Elispot standardization was sought using a reference peptide pool of 23, 8-11 mer epitopes from Influenza, cytomegalovirus (CMV), and Epstein Bar Virus (EBV) presented by 11 common HLA class I molecules.
- 15/17 (88%) HIV- and 14/20 (70%) HIV+ individuals reacted with this test set and *in vitro* simulation of the PBMC from these individuals were capable of killing cells expressing the target antigen.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human, macaque

Keywords dynamics, HAART, ART
References Wodarz 2002

- Mathematical modeling is used to support the idea that T-helper cell dysfunction results in a compromised ability to maintain an anti-HIV CTL memory response. Models suggest strategies to restore CTL memory through therapy and improve long-term immunological control of the virus.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine

Species (MHC) human
Keywords review
References Zinkernagel 2002

- HIV immunity and vaccine strategies are compared with to other pathogens. We do not have a successful vaccine agains TB leprosy, HIV, HCV and most parasites, and the author suggests this is associated with the need for a strong T-cell response to these diseases. Vaccine strategies that achieve a physiological low does infection that is well controlled but persists may be required to alter the immunopathological consequences of infection with HIV.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC) human
Keywords review, inter-clade comparisons, epitope processing
References Gaschen *et al.* 2002

- The concept of using an artificial consensus sequence for vaccine design is discussed, comparing the concepts of a model ancestor sequence or a consensus sequence, with illustrations of the potential advantages of the strategy based on C-clade comparisons.
- See also a comment Nickle *et al.* [2003], and reply Gao *et al.* [2003]

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human, macaque
Keywords review, class I down-regulation by Nef, escape
References Johnson & Desrosiers 2002

- Reviews evidence for CTL escape in HIV epitopes in natural human infections, and in SIV infections of macaque where viral clones with a known time of infection and multiple animals with the same HLA molecules can be tracked.
- Vigorous CTL responses are made despite class I down-regulation by the Nef protein, but it may delay cytolysis of infected cells. Too great a loss of MHC proteins may enhance NK cell killing so the fitness advantage of this function of Nef may be in balance.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine

Species (MHC) human
Keywords review, epitope processing, supertype, computational epitope prediction, HIV exposed persistently seronegative (HEPS), supervised treatment interruptions (STI), immunodominance
References Newman *et al.* 2002

- This extensive review covers many aspects of T-cell immunity and natural HIV infections, and considers how this knowledge might be applied to a polyepitope vaccine approach. Strategies concerning ways to avoid the creation of junctional epitopes and use of linkers to enhance processing of such constructs are discussed.
- The C-terminal flanking residue (C1) was found to be associated with immunodominance of epitopes, such that R or K (positive charge) > N or Q (amide) > C, G, A, T, S (small) > F, W, Y (aromatic) > I, L, M, V (aliphatic) > D (negative). As this position is outside and proximal to the epitope, processing and cleavage is the likely reason for this observation.
- Changing the C1 residue from F to K for an HLA-A2 presented epitope from HBV resulted in a change from the epitope being non-immunogenic to strongly immunogenic.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine

Species (MHC) human
Keywords review, HIV exposed persistently seronegative (HEPS)
References Johnston & Flores 2001

- Reviews the current state of HIV vaccine approaches, and discusses the role of CTL induced immunity in protection or partial protection in animal studies, likening it to the CTL found in HEPS studies.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords binding affinity, review, escape
References Klenerman *et al.* 2002

- The importance of breadth, or spread, of CTL responses is discussed, as narrowly focused responses can be more readily escaped.
- Some HLA types and specific epitope recognition may be associated with a better disease outcome. Reasons for this are considered, including NK cell activity, epitope affinity, epitope conservation, and class I specific induction of more effective T-cell receptors.

HXB2 Location HIV-1
Author Location
Epitope

Immunogen HIV-1 infection
Species (MHC) human
Keywords review, HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission
References Kuhn *et al.* 2002

- Intrauterine exposure of infants to HIV from their mothers results in HIV-1 specific T-helper cell proliferative responses in 1/3 of exposed uninfected babies, and HIV-1 specific CTL in some. Such responses are evident, but it is unknown whether they are associated with lack of infection, but there is some evidence that HIV-1 T-cell responses may reduce transmission in breastfeeding mothers. Summary tables are provided of CD4 and CD8 responses detected in earlier studies.

HXB2 Location HIV-1
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HIV exposed persistently seronegative (HEPS), mother-to-infant transmission
References Kuhn *et al.* 2002; Levy *et al.* 1998

- A non-HLA-specific, non-chemokine-mediated CD8+ T-cell non-cytotoxic anti-HIV response, measured by suppression of acute viral infection of CD4 cells, was detectable in approximately 16/31 (52%) of uninfected children born of infected mothers, was more commonly detected in those <1 year old, and could reflect a protective response.
- Reviewed in Kuhn *et al.* [2002].

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC) human
Keywords dynamics
References Altes *et al.* 2001

- Mathematical modeling suggests if the effector CTL vaccine response exceeds the level of response seen in chronic infection, that a memory CTL population is established that can respond very quickly to protect from infection.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC) human
Keywords review
References Copeland 2002

- This review summarizes cytokines and chemokines produced by CD8+ T-cells that can interfere with HIV's infection and replication.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC)
Keywords review
References Edgeworth *et al.* 2002

- This review summarizes HIV vaccine strategies, adjuvants, current clinical trials and animal models.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC)
Keywords review
References Graham 2002

- This review summarizes HIV vaccine approaches and clinical trials.

HXB2 Location HIV-1
Author Location Env (HXB2)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade HXB2 *HIV component:* gp140ΔCFI, gp160 deletions
Species (MHC) guinea pig, mouse
References Chakrabarti *et al.* 2002

- Intramuscular injection of plasmid DNA was used to vaccinate BALB/c or Huntley guinea pigs with a series of codon-optimized modified HIV-1 HXB2 envelopes – modifications included elimination of glycosylation sites, deletions, and exchange of the V3 loop to change from a X4 or R5 phenotype.
- The mutant envelope gp140deltaCFI gave the most promising result, enhancing antibody responses while retaining the ability to stimulate a strong CTL response.
- gp140deltaCFI has deletions in the cleavage site, fusogenic domain and spacing of the heptad repeats, and was designed to mimic a fusion intermediate.

HXB2 Location HIV-1
Author Location Env (gp160) (384–467)
Epitope
Immunogen Vaccine
Vector/Type: hepatitis B surface antigen lipoprotein particles (HsBAg) *Strain:* B clade LAI *HIV component:* V3
Species (MHC) macaque, rabbit
References Michel *et al.* 1993

- Immunization with recombinant HIV1 V3/HBsAg hybrid particles into rabbits or macaques elicited and maintained for several months anti-V3 or HIV-1 Env proliferative, CTL and Ab responses.

HXB2 Location HIV-1
Author Location Gag (HXB2)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human

References Garba *et al.* 2002

- CD8+ Tcells from 25% of HIV positive individuals produce TGF-beta1 in response to stimulation with HIV proteins, and this can significantly reduce CD8+ T-cell IFN-gamma induction to HIV and vaccinia proteins.
- Different peptides can preferentially induce TGF-beta1 or IFN-gamma from CD8+ T-clymphocytes from the same individual, and TGF-beta1 non-specifically suppresses HIV-specific immune responses.

HXB2 Location HIV-1
Author Location Pol (HXB2)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Garba *et al.* 2002

- CD8+ Tcells from 25% of HIV positive individuals produce TGF-beta1 in response to stimulation with HIV proteins, and this can significantly reduce CD8+ T-cell IFN-gamma induction to HIV and vaccinia proteins.
- Different peptides can preferentially induce TGF-beta1 or IFN-gamma from CD8+ T-clymphocytes from the same individual, and TGF-beta1 non-specifically suppresses HIV-specific immune responses.

HXB2 Location HIV-1
Author Location Env (MN)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Garba *et al.* 2002

- CD8+ Tcells from 25% of HIV positive individuals produce TGF-beta1 in response to stimulation with HIV proteins, and this can significantly reduce CD8+ T-cell IFN-gamma induction to HIV and vaccinia proteins.
- Different peptides can preferentially induce TGF-beta1 or IFN-gamma from CD8+ T-clymphocytes from the same individual, and TGF-beta1 non-specifically suppresses HIV-specific immune responses.

HXB2 Location HIV-1
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords assay standardization/improvement, acute infection
References Altfeld *et al.* 2003

- The frequency of HIV-1 specific T-cell responses was characterized in an Elispot IFN-gamma assay, using 507 overlapping peptides based on the B clade consensus sequence spanning all HIV-1 clade B proteins against PBMC from 57 HIV-1 infected patients at various disease and treatment stages. 63% of the peptides were recognized (range of 1-42 per subject, median=14). More variable peptides were targeted less frequently.
- Autologous virus sequences from six patients in acute infection spanning of HIV-1 p24, Tat and Vpr were used to scan for missed responses due to viral variation when using the consensus for peptides. 12/42 (29%) responses to these peptides were dectected only with autologous peptides, and often these autologous reponses were immunodominant. Responses were also generally higher using autologous peptides.
- A longitudinal analysis (5 yrs) of the T-cell responses in 5 patients showed that the autologous sequence detected stronger T-cell recongition than the HIV-1 clade B consensus sequence.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) chimpanzee
Keywords review
References Balla-Jhagjhoorsingh *et al.* 2003

- This paper reviews HIV-1-specific cell-mediated immune responses in chimpanzees and discusses mechanisms that might control HIV-1 pathogenesis in chimpanzees. During the first decade of the HIV epidemic, more than 200 chimpanzees were experimentally infected with HIV. Among these only one case of declining CD4+ cells has been reported, all others have remained asymptomatic with no loss of immune function , some after 20 years of infection. In contrast to infected humans which have a skewed Th2 response, chimpanzees maintain balanced Th responses and are likely to support a fully mature CD8+ T-cell response.
- Specific HIV epitopes recognized by chimpanzees have been mapped and CTL detected , but overall the responses are at much lower levels than in humans, as viral loads are so low. Gag epitope responses are estimated to be 0.0095 to 0.0025% of the CD8+ T cell population in chimpanzee, and 1-2% in humans.
- The authors argue that the chimpanzee immune response may be effective at controlling virus because it focuses on conserved epitopes, and further speculate that long contact with lentiviruses may have put strong selection pressures on the chimpanzee MHC class I, narrowing the population's ability to respond to only the most conserved, and so useful, epitopes.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ
Keywords HAART, ART, supervised treatment interruptions (STI)
References Fagard *et al.* 2003

- This study monitored the effects of repeated treatment interruptions (STI), in 2-week intervals, in 133 HIV-1 infected, HAART-treated patients. STIs were rarely able to control viremia without continued HAART, and increases in CD8+ T-cell response frequencies did not correlate with the level of control of viral replication. CD8+ T cell responses were measured by gamma IFN Elispot using between 2-32 different optimal HIV epitopes, selected to be appropriate for the patient's HLA type.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen
Species (MHC) human
References

HXB2 Location HIV-1
Author Location HIV-1
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ
Keywords responses in children
References Feeney *et al.* 2003

- The magnitude and breadth of CD8+ T-cell responses in 18 pediatric (6-17 years) perinatally HIV-1 infected patients was determined using 1) overlapping peptides spanning all HIV-1 proteins and 2) peptides from all predefined appropriately class I HLA-restricted HIV-1 epitopes.
- Perinatally infected children's CD8+ T-cell responses were comparable in magnitude and breadth to adult responses. Many reactive peptides did not overlap with a previously characterized optimal epitope.
- On average 20% of all known pre-defined optimal epitopes presented by appropriate HLAs were recognized in these children. In two patients, autologous sequences spanning unrecognized potential epitopes usually corresponded to the reactive form of the epitope, so epitope variation alone did not account for unrecognized epitopes.
- Children with detectable viremia showed a broader and greater CTL responses than HAART responsive children with undetectable viremia.

HXB2 Location HIV-1
Author Location HIV-1
Epitope
Immunogen
Species (MHC)
References

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC)
Keywords review
References Hanke 2003

- Review of HIV vaccine development discussing diversity, the merits and difficulties of stimulating different arms of the immune response, and different strategies, including DNA vaccines, viral vectors, CTL epitope based, and protein- or peptide-based vaccines.

HXB2 Location HIV-1
Author Location HIV-1 (HXB2)
Epitope
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Hladik *et al.* 2003

- Longitudinal study analyzed IFN-γ CD8+ T cell responses in highly exposed, seronegative homosexual men. Overlapping peptides spanning the Gag, Env, Nef and Pol subtype B HXB2 sequence were used to stimulate PBMC from 26 individuals, whose frequency of HIV-1 specific IFN-γ T cell responses were very low.
- CD8+ T cells from 3/15 individuals (EES15, ES29, and ES63) recognized > 3 peptide pools.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type Chromium-release assay
Keywords dynamics
References Kousignian *et al.* 2003

- The diversity of HIV protein (Gag, Pol, Env, Nef, Rev, Tat, Vif) recognition by CTLs was studied longitudinally in a cohort of 152 HIV-infected untreated individuals, and was analyzed by Markov modelling. CTL responses from 152 HIV-1 infected patients in four stages of disease progression were collected for a period of 5 years. Results show that memory CTL responses against HIV-1 proteins are acquired during early HIV-1 infection and subsequently lost. As viral load increased there was an accelerating loss of multiple protein recognition.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: gp120 depleted whole killed virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human
References Lederman & Douek 2003; Robbins *et al.* 2003

- Lederman and Douek is an editorial comment referring to the study presented by Robbins *et al.*, in which the authors discuss why an HIV-1 gp120-depleted inactivated HIV vaccine elicits HIV-1 specific T helper responses in 5/5 HIV+ people, but not CD8+ CTL responses. In chronically infected people it appears that stimulating Th responses in and of itself is not enough to restore strong CTL responses.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine
Adjuvant: E. coli mutant heat labile enterotoxin (LT-R72), CpG immunostimulatory sequence (ISS), HSP70
Species (MHC) human
Keywords review, Th1, Th2, genital and mucosal immunity
References Lehner 2003

- This review discusses the importance of mucosal and innate immunity for future vaccination strategies in HIV infection in humans. Different mucosal adjuvants are compared, and the advantages of a Th1 polarized response.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Onyemelukwe & Musa 2002

- Longitudinal study (1991-1997) of the clinicial presentation of 80 HIV-1 or HIV-II seropositive people in Zaria, Nigeria, who contracted HIV-1 primarily via heterosexual transmission. Main complicating diseases were tuberculosis and bacterial infections including Salmonella, Streptococcus peneumoniae and Stahhylococcus. HIV-1 progression was associated with a decline of not only CD4+ T cells, but CD8+ T cells as well – patients had CD4+ counts < 200 cells/ul, and CD8 counts were 190 cells/ul versus 440 cells/ul for controls.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Onyemelukwe & Musa 2002

- Longitudinal study (1991-1997) of the clinicial presentation of 80 HIV-1 or HIV-II seropositive people in Zaria, Nigeria, who contracted HIV-1 primarily via heterosexual transmission. Main complicating diseases were tuberculosis and bacterial infections including Salmonella, Streptococcus peneumoniae and Stahhylococcus. HIV-1 progression was associated with a decline of not only CD4+ T cells, but CD8+ T cells as well – patients had CD4+ counts < 200 cells/ul, and CD8 counts were 190 cells/ul versus 440 cells/ul for controls.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords HAART, ART
References Price *et al.* 2003

- CD4+ and CD8+ T cell responses were analyzed in this longitudinal study (19 mo) of 53 patients with chronic HIV-1 infection receiving continous ART therapy. Three subgroups were compared: one with suppressed viremia and increasing CD4+ T cell counts, one with dectable viral load and declining CD4, and one with detectable viral load with a positive CD4+ T cell slope.
- IFN-γ ELISPOT analysis was performed with peptides spanning RT, Env, Gag (p24), Gag(p17), Nef, Tat and Rev. The IFN-γ analysis showed the greatest CD4+ as well as CD8+ T-cell responses in the group with stable CD4+ T cell responses despite detectable virus over a median time course of 9 months.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen
Species (MHC) human
Assay type Chromium-release assay
Keywords rate of progression
References Sindhu *et al.* 2003a; Sindhu *et al.* 2003b

- In a cross-sectional study of 31 HIV+ people, a correlation was observed between CTL-mediated bystander HLA-unrestricted lysis of primary CD4+ T-cells. $\gamma\delta$ CTL are abnormally expanded in HIV+ people, and the Vδ1 subset can deplete bystander CD4+ T-cells and expedite progression. In a set of 13 patients, an inverse correlation was observed between CD8+ T-cell activation markers and viral load, thought to be an indicator of CTL-associated immunopathogenesis in HIV progression.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC)
Keywords review
References Vella & Daniels 2003

- This article reviews the CD8+ T-cell antiviral factor (CAF). CAF contributes to MHC restricted, CD8+ T-cell mediated non-cytolytic suppression of HIV in infected individuals.

HXB2 Location HIV-1
Author Location
Epitope
Subtype A, B, C
Immunogen Vaccine
Vector/Type: DNA, polyepitope *HIV component:* gp120, gp41, Nef, p17 Gag, p24 Gag, Pol *Adjuvant:* concavalin A-immobilized polystyrene nanospheres
Species (MHC) mouse
Assay type proliferation, CD8 T-cell Elispot - IFNγ
Keywords vaccine-induced epitopes
References Bazhan *et al.* 2004

- A synthetic T cell polyepitope immunogen containing 80 overlapping Env, Gag, Pol and Nef epitopes was used to immunize mice. It induced both humoral and cellular responses which increased upon reimmunization.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen
Species (MHC)
Keywords review, class I down-regulation by Nef, early-expressed proteins, immune evasion
References Collins 2004

- There are a number of factors that combined make HIV-infected cells resistant to CTLs. HLA-associations with disease progression are reviewed. Nef down-regulation of HLA class I A and B molecules is one important mechanism of HIV immune evasion. Rev allows late viral proteins to be expressed, enabling CTL specific for epitopes in these proteins to recognize infected cells. It is suggested that blocking the activity of Nef

and Rev would reduce production of viral variants and enhance the ability of CTLs to combat HIV.

HXB2 Location HIV-1
Author Location (SIV)
Epitope
Immunogen SIV infection
Species (MHC) macaque
Keywords escape, reversion, viral fitness
References Friedrich *et al.* 2004

- SIV CTL escape variants revert to wild-type epitopes after transmission to new hosts with disparate MHC class I alleles. Thus mutations in CTL epitopes may have moderate to severe negative effects on viral replicative fitness although some escape variants are shown to accumulate substitutions in flanking regions of the epitope that help compensate for fitness loss.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen
Species (MHC) human
Keywords dynamics, HAART, ART
References Ganusov 2003

- The rate of virus decline after initiation of HAART is shown by a mathematical model, to depend on whether the virus is controlled by the CTL response via lytic or non-lytic mechanisms.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords review, class I down-regulation by Nef, escape, dendritic cells, TCR usage, memory cells, immune dysfunction
References Gulzar & Copeland 2004

- HIV has developed numerous strategies to evade CD8+ T-cell response that are reviewed in this paper, including escape mutations in CD8+ T-cell recognition, down-regulation of MHC-I surface expression, alternating cytokine production, disruption of proper CD8+ T-cell signaling resulting in anergy, and disruption of the function of CD4+ T-cells and APCs required for CD8+ T-cell maturation.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen in vitro stimulation or selection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay
Keywords characterizing CD8+ T cell responses
References Kitchen *et al.* 2004

- This paper characterizes a population of cells that are CD3+, CD8+, and CD4+. These cells are mature and highly activated. The CD4 molecule expressed by these CD8+ T-cells plays an important role in expression of IFN-gamma and Fas ligand and cytotoxic responses. HIV infection of CD8+CD4+ T-cells results in Nef independent down-regulation of CD4 and dysregulation of IFN-gamma and Fas ligand, and provides an additional resevoire for the virus.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen
Species (MHC) human
Keywords review, characterizing CD8+ T cell responses
References Petrovas *et al.* 2004

- This review discusses the attributes of HIV-specific CTLs that contribute to their inability to control HIV infection, with an emphasis on the susceptibility of HIV-specific CTL to CD95/Fas induced apoptosis upon binding target cells. Furthermore, Nef may inhibit apoptosis by blocking CD95/Fas signaling on infected cells.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Country United Kingdom.
Assay type proliferation, CD8 T-cell Elispot - IFNγ, T-cell Elispot, Flow cytometric CTL assay
Keywords HAART, ART, immune dysfunction
References Pires *et al.* 2004

- Daily administration of rec human growth hormone (rhGH) induced an increase in the numbers of naive CD4 T-cells and effector CD8 T-cells. Also, a rise in HIV-1 antigen-specific CD4 and CD8 T-cell responses was observed. The function of specific effector CD8 T-cells was perserved despite an eventual decrease of specific CD4 T-cell responses.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine

Species (MHC) human
Country United States.
Assay type CD8 T-cell Elispot - IFNγ
Keywords review, supervised treatment interruptions (STI), vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization
References Robinson 2003

- This paper is a commentary on Altfeld et al, Nature 420:434 2002. The patient AC-06 was superinfected with a second strain of HIV-1 after STI despite 12 of 25 recognized CD8+ T-cell epitopes maintaining strong cross-reactive immunity measured by gamma IFN EliSpot against the second strain. While vaccine trials in macaques have given optimistic results, this patient's superinfection in spite of a strong cross-reactive CD8+ T-cell immune response suggests that vaccine strategies may have to be re-examined.

HXB2 Location HIV-1
Author Location
Epitope

Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country Spain.
Assay type Flow cytometric CTL assay
Keywords rate of progression
References Rodés *et al.* 2004

- A complex set viral or host factors has been found to be associated with the absence of disease progression among long-term non-progressors (LTNP). 19 LTNP were followed for six years; 12 were non-progressors over this period, 7 showed a slow progressive CD4 depletion. Their virus replicative capacity was shown to be reduced and T-cell activation was low. Pooled peptide CD8+ T-cell gamma IFN responses did not differ between non-progressors, slow progressors, or a group of HIV progressors.

HXB2 Location HIV-1
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection, Vaccine
Vector/Type: canarypox prime with recombinant protein boost *Strain:* B clade SF2 *HIV component:* Env, Gag, Protease
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords assay standardization/improvement
References Russell *et al.* 2003

- IFNγ Elispot assay is shown to be a good initial screening method for measurment of CD8+ T-cell responses in both vaccination and natural HIV-1 infection. Responses were detected using peptides at low concentrations (1-2 µg/mL) and an increase in detection of HIV-1 specific CD8+T-cells by using 15-mers rather than 20-mer peptides for cell activation was observed. More responses were detected using smaller pools (10 or 2 peptides) than larger pools (25 or 50 peptides), so smaller pools may be needed to detect low frequency responses. Responses to natural infection were more than a log higher than to the vaccine.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, SIV infection
Species (MHC) human, macaque
Keywords review, escape, reversion, viral fitness
References Smith 2004

- This paper reviews several studies which track HIV and SIV CTL escape mutations after transmission into a new host, and reversion rates and fitness costs of CTL escape. Some escape mutants have a cost to viral fitness. The author suggests that CTL based HIV-1 vaccine should therefore not only increase cellular responses against viral epitopes but also favor epitopes where escape mutations result in significant decrease in viral fitness.

HXB2 Location HIV-1
Author Location
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade *HIV component:* gp140, gp160 *Adjuvant:* reovirus alpha 1 protein
Species (MHC) mouse
Donor MHC H-2d
Assay type cytokine production, Chromium-release assay
Keywords adjuvant comparison
References Wang *et al.* 2003

- M cells are found in the follical-associated epithelium in mucosal inductive tissues, and reovirus are able to attach to these cells via the alpha 1 protein. Respiratory mucosal sites were targeted with a reovirus protein alpha 1 protein delivered with a DNA vaccine administerd i.n. in BALB/c mice. The naked gp160 DNA vaccine did not elicit CD8+ T cell reponses, but when delived with alpha 1 protein, CTL responses were observed in the lungs, spleens and lymph nodes. gp160 was shown to be most immunogenic compared to a cytoplasmic gp140 and secreted gp140. The vaccinated animals had reduced vaccinia virus when challeneged with a vaccinia-env recombinant.

HXB2 Location HIV-1
Author Location Gag
Epitope
Immunogen Vaccine
Vector/Type: DNA with CMV promotor, fowlpoxvirus *Strain:* SIV *HIV component:* Env, Gag, Pol, Rev, Tat, Vpu *Adjuvant:* IFNγ, CpG immunostimulatory sequence (ISS)
Species (MHC) macaque
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords adjuvant comparison, vaccine antigen design
References Dale *et al.* 2004

- Macaques immunized with DNA and fowlpox vaccines showed high levels of CD4 and CD8 T-cell immune responses to Gag. Single DNA priming vaccination or coexpressed IFN-gamma with the fowlpox virus boost were shown to be less immunogenic and less protective than sequental DNA and fowlpox virus vaccination. Partial protective immunity was observed following a high dose, virulent SHIV challenge, for the DNA fowlpox prime boost, as well as the DNA vaccination alone, even though standard assays failed to detect a strong immune respsonse with DNA alone.

HXB2 Location HIV-1
Author Location (IIIB, Thai B', Chinese CB)
Epitope
Subtype B, C
Immunogen HIV-1 infection
Species (MHC) human
Country China.
Assay type Intracellular cytokine staining, Chromium-release assay
Keywords inter-clade comparisons, characterizing CD8+ T cell responses

References François-Bongarcon *et al.* 2004

- The ability of circulating T-cells from 7 North American and 4 Chinese HIV+ donors to produce IFN-gamma and/or lyse autologous primary cells infected with HIVIIIB, B' (Thai B) or C/B recombinant form was tested. The results showed cross-clade CD8 T-cell responses to the Cinese viruses among North American donors and to HIVIIIB in Chinese donors, suggesting that many of the T-cell responses to clade B virus epitopes are conserved across clades. Lysis of cells by N. American donor CD8+ T cells infected with IIIB or a Thai B' strain were comparable, while lysis infected with the Chinese BC recombinant was somewhat reduced, although the reduction was not statistically significant.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Country Canada.
Assay type cytokine production, Chromium-release assay, Flow cytometric CTL assay
Keywords TCR usage, memory cells, characterizing CD8+ T cell responses, immune dysfunction
References Gamberg *et al.* 2004b

- A relationship was found between the proportion of HIV-specific CTLs expressing CD28 and CD4+ T-cell counts, viral load and disease progression. This association cannot be linked to disease related degeneration of CD8+CD28- T-cells in terms of their TCRbetaV family repertoire diversity or ability to produce cytokines. This suggests that effective immune responses contain CD8+CD28+ T-cell populations that shift to CD8+CD28- in ineffective responses.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen
Species (MHC)
Keywords review, epitope processing, vaccine-specific epitope characteristics, rate of progression, immunodominance, escape, acute infection, early-expressed proteins, TCR usage, reversion, viral fitness
References Goulder & Watkins 2004

- CTLs have a central role in the control of HIV infection. Emergence of escape variants to CTLs is one of the major obstacles to vaccine development. Factors that should be considered for the development of an HIV vaccine are CTLs that are specific for epitopes recognized during the acute phase of infection, CTLs that are able to efficiently control viral replication, and epitopes from regions of the viral genome that are highly conserved or where variation results in loss of viral fitness.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Country Kenya.
Assay type Chromium-release assay
Keywords HIV exposed persistently seronegative (HEPS), characterizing CD8+ T cell responses
References Kaul *et al.* 2004

- HIV-1 specific CTL responses found in HIV exposed persistently seronegative Kenyan female sex workers were shown to be associated with age and recent HIV-1 exposure, but not with protection against HIV-1 infection. The authors note that CTL may be the result of a non-productive HIV infection, but not mediate protection; alternatively, the low incidence, possibly due to behavioral interventions, may not give adequate sampling to detect the response.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Country France.
Keywords HAART, ART, characterizing CD8+ T cell responses, immune dysfunction
References Kryworuchko *et al.* 2004

- A subset of HIV-1 infected untreated patients had CD8+ T-cells that were unable to respond to IL-2 by activating STAT5a and b proteins. This was correlated with an impaired activation of the upstream kinase Jak-3. 6 months of HAART was shown to restore Jak/STAT signalling in those patients and their CD8+ T-cell response to IL-2. This suggests another mechanism for immune dysfunction in HIV infected patients.

HXB2 Location HIV-1
Author Location
Epitope
Subtype A, B, C, D, F, G, U
Immunogen computer prediction
Species (MHC) human
Keywords vaccine antigen design
References Maksyutov *et al.* 2004

- Every HIV protein was shown to have some regions that were highly similar to the regions of human proteins. Most of those regions contained T-cell or/and B-cell epitopes. The epitopes shared by HIV and its host may have immunopathogenic potential through stimulating autoimmunity and should possibly be excluded from HIV vaccines. All HIV proteins from the sequence of BH10 were compared to human proteins, as well as many HIV-1 V3 variants.

HXB2 Location HIV-1
Author Location (ELI)
Epitope
Immunogen in vitro stimulation or selection
Species (MHC) human
Assay type cytokine production, proliferation, Chromium-release assay, Flow cytometric CTL assay
Keywords class I down-regulation by Nef, rate of progression, dendritic cells, immune dysfunction
References Quaranta *et al.* 2004

- Exogenous Nef protein activates immature DCs and inhibits the capacity of DCs to prime CD8+ T-cell responses by down-regulating their proliferation and function capacities. Nef induces CD8+ T-cell apoptosis by up-regulating TNF-alpha and FasL production by DCs, while DCs are protected from apoptosis themselves. These mechanisms, as well as by down regulation of the HLA class I proteins, can contribute to HIV-triggered immune dysfunction.

HXB2 Location HIV-1
Author Location
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country Switzerland.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords rate of progression
References Oxenius *et al.* 2004a

- In untreated, HIV-1 chronically infected patients, CD4+ T-cell responses and, to a lesser extent, CD8+ T-cell responses, were found to inversely correlate with disease progression rate. Polymorphisms in CCR genes, HLA genotype and GB virus C coinfection were not found to be related to slower disease progression.

HXB2 Location HIV-1
Author Location (B clade)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country Canada.
Assay type CD8 T-cell Elispot - IFNγ, Flow cytometric CTL assay
Keywords genital and mucosal immunity, characterizing CD8+ T cell responses
References Sheth *et al.* 2004

- HIV viral load in semen is found to be 10-fold lower than in blood. No correlation was found between viral load in either semen or blood and systemic HIV-specific CD8 T-cell responses, in 20 samples.

HXB2 Location HIV-1
Author Location
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA with CMV promotor, virus-like particle (VLP), modified vaccinia Ankara (MVA) *Strain:* B clade *HIV component:* Env, Gag, Pol, Protease, RT
Species (MHC) macaque
Assay type T-cell Elispot, Intracellular cytokine staining
Keywords vaccine antigen design
References Smith *et al.* 2004

- Macaques were immunized with codon-optimized Gag DNA and non-codon-optimized Gag-Pol-Env DNA vaccines, expressed as VLPs as aggregates, followed by an MVA boost. There was no significant difference in anti-Gag T-cell responses and anti-Env Ab responses between the different vaccines. A second MVA boost did not increase T-cell responses but it increased anti-Env Ab titers by 40- to 90-fold.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen
Species (MHC) human
Keywords review, epitope processing, rate of progression, escape, early-expressed proteins, vaccine antigen design
References Yang 2004

- This review considers CTL biology in HIV infection in the context of vaccine design principles. Since HIV-1 infection damages immunity through depletion of CD4+ T-cells, which in turn results in diminished capacity of the immune system to produce new and functional CTL responses, maximizing the breadth of CTL responses might not be enough for an HIV-1 vaccine. CTLs recognizing early proteins might be more prone to epitope escape mutation, while those recognizing more conserved structural proteins might be more likely to persist, so focusing on more conserved proteins those might be a good strategy to produce an attenuating vaccine.
- Original antigenic sin is discussed, the initial responses to an antigen that persist even after escape occurs, blunting the later immune response. If the goal is to prevent disease, focusing on conserved late expressed proteins might be the best target, where the fitness cost is greatest for escape; if the goal is to prevent infection, focusing the vaccine on the more variable early expressed proteins that elicit the first responses, Tat and Nef, might be best.

HXB2 Location HIV-1
Author Location p24 (HIV-2 ROD, HIV-1 IIIB)
Epitope
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human
Country Gambia.
Assay type cytokine production, proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords rate of progression
References Jaye *et al.* 2004

- A comparison of T cell responses in HIV-1 and HIV-2 infected asymptomatic patients with CD4+ cell counts 20% showed no significant difference between groups. Viral loads were roughly 20 times greater in HIV-1 positive patients than HIV-2 positive patients.
- 10/20 (50%) of HIV-1 infected patients demonstrated proliferative responses with SI greater than 1.4 to gp120, and 11/20 to p24. 8/29 (29%) of HIV-2 infected patients recognized gp105, and 8/29 (29%) p26. Cytokine responses in both groups did not differ.
- 9/21 (43%) of HIV-1 + and 15/30 (50%) of HIV-2 + patients had cyotoxic T cell responses to Gag, and 3/21 (14%) HIV-1 + and 8/30 (27%) HIV-2 + responded to Pol.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Country Spain.
Assay type proliferation, Intracellular cytokine staining
Keywords HAART, ART
References López *et al.* 2004

- A clinical trial compared chronically HIV-1 infected patients who had replaced HAART with didanosine (ddI) and hyroxyurea (HU) were followed for 12 months to an untreated HIV+ group and a group that continued on HAART.
- Approximately 20% of the patients treated with ddI-HU had detectable CD4+ T-cell proliferative responses to Gag and Env in contrast to drug-naive and HAART treated HIV-infected patients, who had few or no responses.
- HIV-specific CD8+ T-cell responses were higher in ddI-HU treated patients than HAART treated patients, even in individuals that maintained undetectable viral loads.

HXB2 Location HIV-1
Author Location
Epitope
Subtype CRF01_AE
Immunogen Vaccine

Species (MHC) human (A11)
Keywords review, vaccine-specific epitope characteristics, escape
References Ariyoshi *et al.* 2002

- This review summarizes a meeting held to discuss options for determining CTL responses to vaccines. Problems are noted: costs for some assays are prohibitive for a Phase III study, Elispot shows interlaboratory variation but could be extended to many samples. HLA-A11 is very common in Thailand – over 30% carry the HLA-A11 allele. Predominant strains may be evolving to evade recognition of A11 restricted epitopes. Few full length CRF01 sequences are available. Epitopes may differ in vaccinees and infected individuals.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human (A11, B8, B40, Cw8)
Assay type cytokine production, CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords HAART, ART, acute infection, early treatment
References Alter *et al.* 2003

- Longitudinal study (24 mo) monitoring T-cell immune responses in 4 patient groups: Group 1 (n=6) consists of subjects who underwent HAART preseroconversion, group 2 (n=11) were HAART treated during early postseroconversion, group 3 (n=5) contained patients who started HAART during late postseroconversion, and group 4 (n= 6) commenced with HAART during chronic HIV-1 infection.
- The experimental strategey was to test for reactivity levels with sets of peptides that each contain epitopes with known HLA-restricting elements, making the peptide selection based on the optimal epitope list in this database. The HLA alleles found in the patients were balanced so that the frequency in the groups were comparable. Peptides spanning parts of Gag, Env, Nef, and RT were used for Elispot, and Gag peptides were used for ICS.
- All group 1 patients, and 5/11 group 2 patients, maintained the breadth and the magnitude of the immune response throughout the study; those in group 2 that maintained response started therapy earlier. The hierarchy of intensity of responses to different peptides was preserved. Individuals in groups 3 and 4 all showed a decline, and after treatment lost responses. Groups 1 and 2 showed HAART-induced suppression of viremia but maintained resposnes. Groups 3 and 4 both showed viral suppression in association with a decreased immune response in breadth and magnitude after HAART. The authors suggest that preservation of HIV CD4+ responses can be maintained even if HAART is first given beyond the acute phase of infection, and a delay may allow a full CD8 response to develop while still allowing CD4 function to be preserved.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC) human (B27, B8)
Keywords binding affinity, review, inter-clade comparisons, epitope processing, escape
References McMichael & Hanke 2002

- CTL response-eliciting vaccines are reviewed. The natural epitope interactions with the HLA class I presenting molecules and T-cell receptors are described, and the impact of breadth of CTL responses and diversity considered in a vaccine context.
- Interesting specific examples are given concerning anchor chain residues. For B27, the B pocket fits Arg (R) but not Lys (K), so even this conservative change is not tolerated. In B8 either R or K can fit in the B pocket, but the substitution will cause conformational shifts in other parts of the epitope.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *HIV component:* Gag
Species (MHC) mouse (H-2^d)
Keywords review
References Lieberman 2002

- Attenuated Listeria monocytogenes vectors elicit strong persistent CTL responses in vaccinations of BALB/c mice and can protect mice from a vaccinia-gag challenge.

HXB2 Location HIV-1
Author Location gp120 (V3) and p24 (IIIB, MN, BH10)
Epitope
Subtype A, B
Immunogen Vaccine

Vector/Type: virus-like particle (VLP) *Strain:* A clade UG5.94UG018, B clade IIIB *HIV component:* Gag, gp120

Species (MHC) mouse (H-2^d)
Assay type Chromium-release assay
Keywords inter-clade comparisons
References Buonaguro *et al.* 2002

- Different HIV strains were used for different regions: gp120 A clade UG5.94UG018, and B clade IIIB
- BALB/c mice were given intraperitoneal immunization with virus-like particle (VLPs) expressing recombinant subtype A gp120 and Pr55gag in the absence of adjuvants.
- High dose-independent humoral responses against both gp120 and p24 peptides were detected. Antibodies able to elicit 50% neutralization against A clade IIIB and the autologous clade a virus were obtained.
- Recombinant rgp120 (clade B, MN) induced T-cell proliferative responses *in vitro* from vaccinated animals.
- CTL activity was observed against splenocytes expressing Env (clade A) and Gag (clade B, BH10) from a vaccinia construct.

HXB2 Location HIV-1
Author Location
Epitope
Subtype B
Immunogen Vaccine

Vector/Type: DNA, polyepitope *Strain:* A clade, B clade *HIV component:* Env, Gag, Pol *Adjuvant:* IL-12, IL-2, liposome

Species (MHC) mouse (H-2^d)
Assay type CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining, Delayed-type hypersensitivity (DTH), Chromium-release assay
Keywords vaccine-induced epitopes
References Shinoda *et al.* 2004

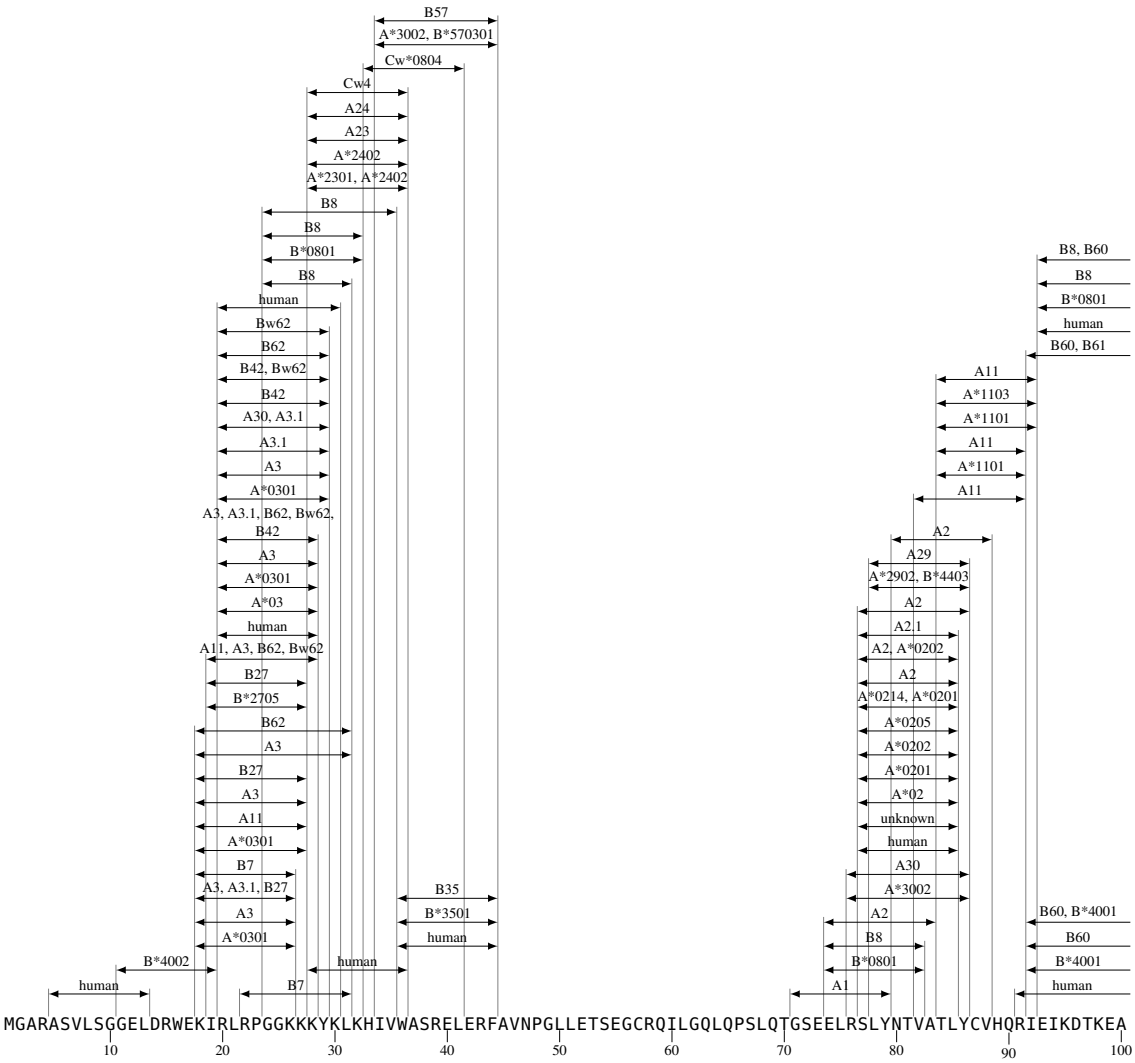
- Mice immunized with a polyepitope DNA vaccine encoding 20 antigenic epitopes of several HIV-1 clades (hDNA vaccine) showed strong Ab responses, activation of IFN-gamma secretion cells targeting gp120 and synthetic antigenic peptides, and several peptide specific CTL responses. When challenged with recombinant HIV-vaccinia viruses, mice immunized with the hDNA vaccine showed lower viral titers in the ovary.

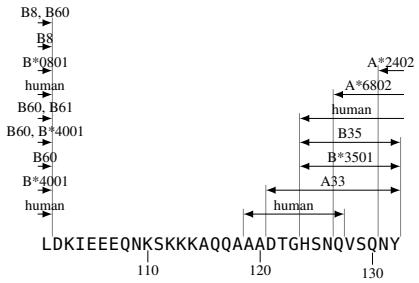
II-C

Maps of CTL Epitope Locations Plotted by Protein

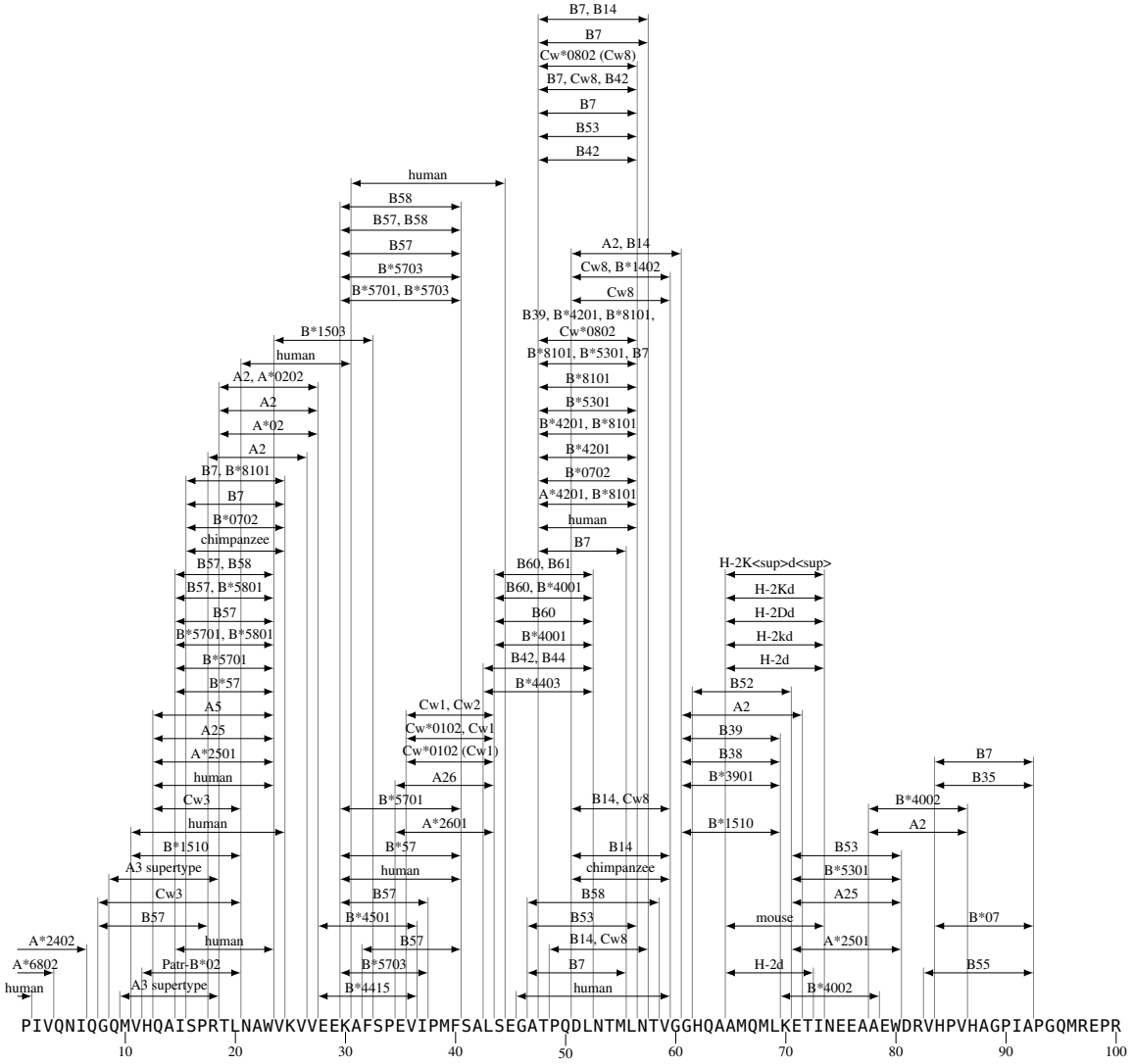
Linear CTL epitopes mapped to within a region of 14 amino acids or less are shown.

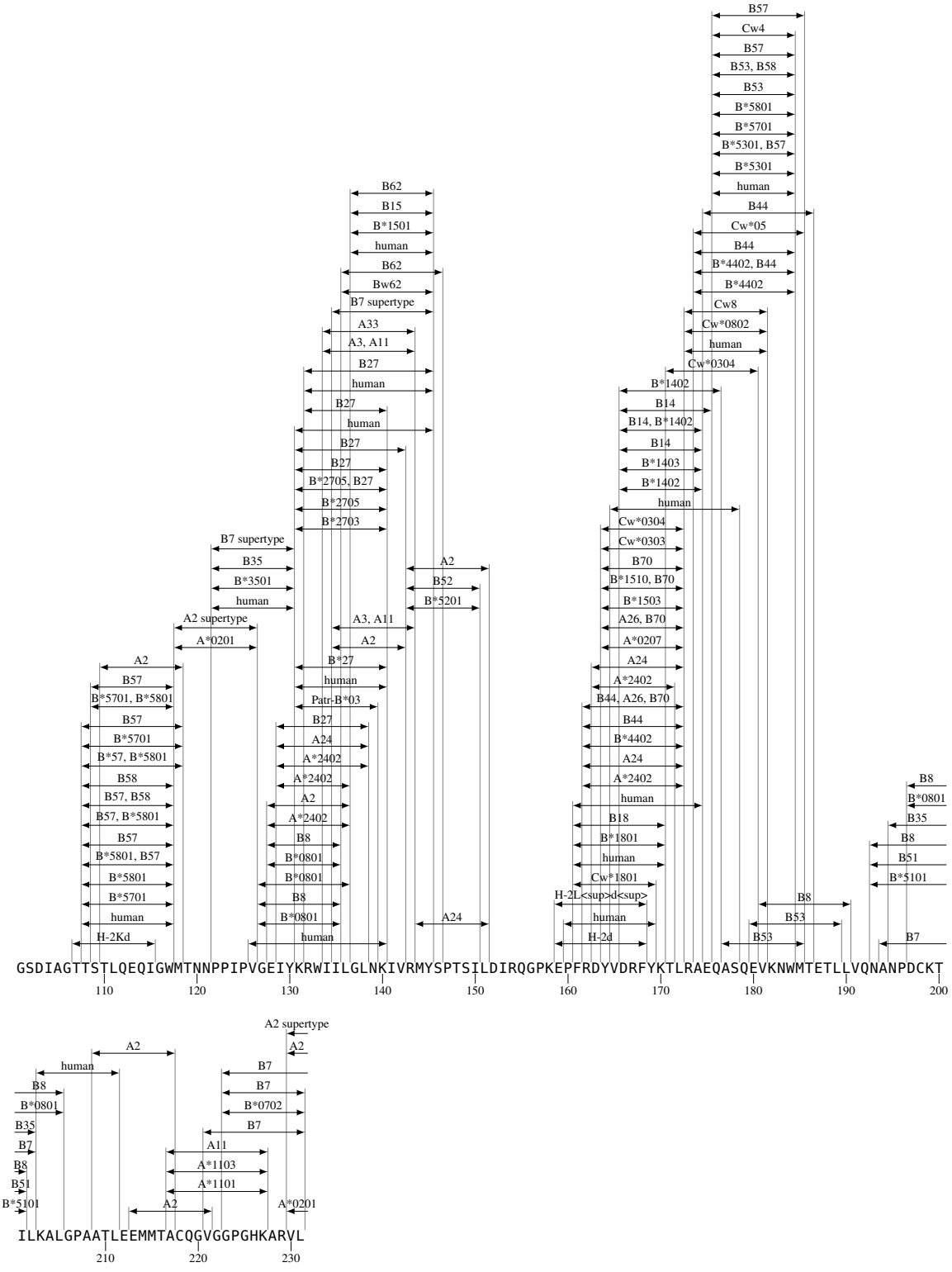
II-C-1 Gag p17 CTL, CD8+, Epitope Map





II-C-2 Gag p24 CTL, CD8+, Epitope Map

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Cw4
B57
B53, B58
B53
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B*5301, B57
B*5301
human
B44
Cw*05
B44
B*4402, B44
B*4402
Cw8
Cw*0802
human
Cw*0304
B*1402
B14
B14, B*1402
B14
B*1403
B*1402
human
Cw*0304
Cw*0303
B70
B*1510, B70
B*1503
A26, B70
A*0207
A24
A*2402
B44, A26, B70
B44
B*4402
A24
A*2402
human
B18
B*1801
human
Cw*1801
H-2L^d
human
H-2d
B62
B15
B*1501
human
B62
Bw62
B7 supertype
A33
A3, A11
B27
human
B27
human
B27
B27
B*2705, B27
B*2705
B*2703
B7 supertype
B35
B*3501
human
A2
B52
B*5201
A2 supertype
A*0201
A3, A11
A2
B*27
human
Patr-B*03
B27
A24
A*2402
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A2
A*2402
B8
B*0801
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B8
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human
A24
H-2Kd
A2
B57
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B8
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B53
B53
B7
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120
130
140
150
160
170
180
190
200
A2 supertype
A2
A2
human
B7
B8
B7
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B*0702
B35
B7
B7
A11
B8
A*1103
B51
A*1101
B*5101
A2
A*0201
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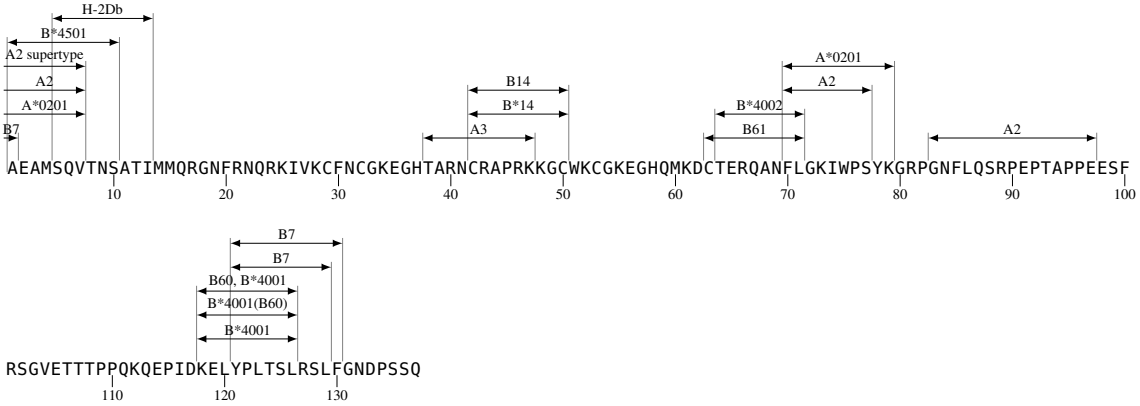
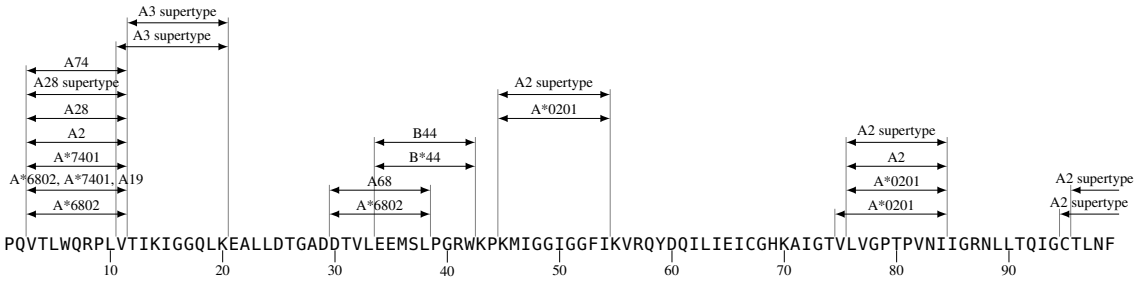
210
220
230

II-C-3 Gag p2p7p1p6 CTL, CD8+, Epitope Map

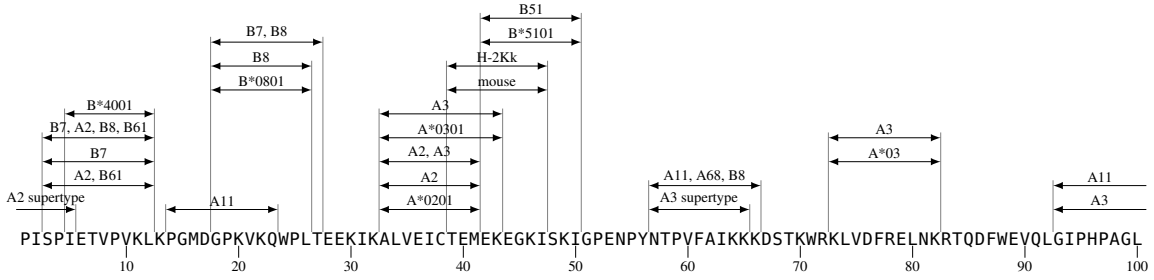


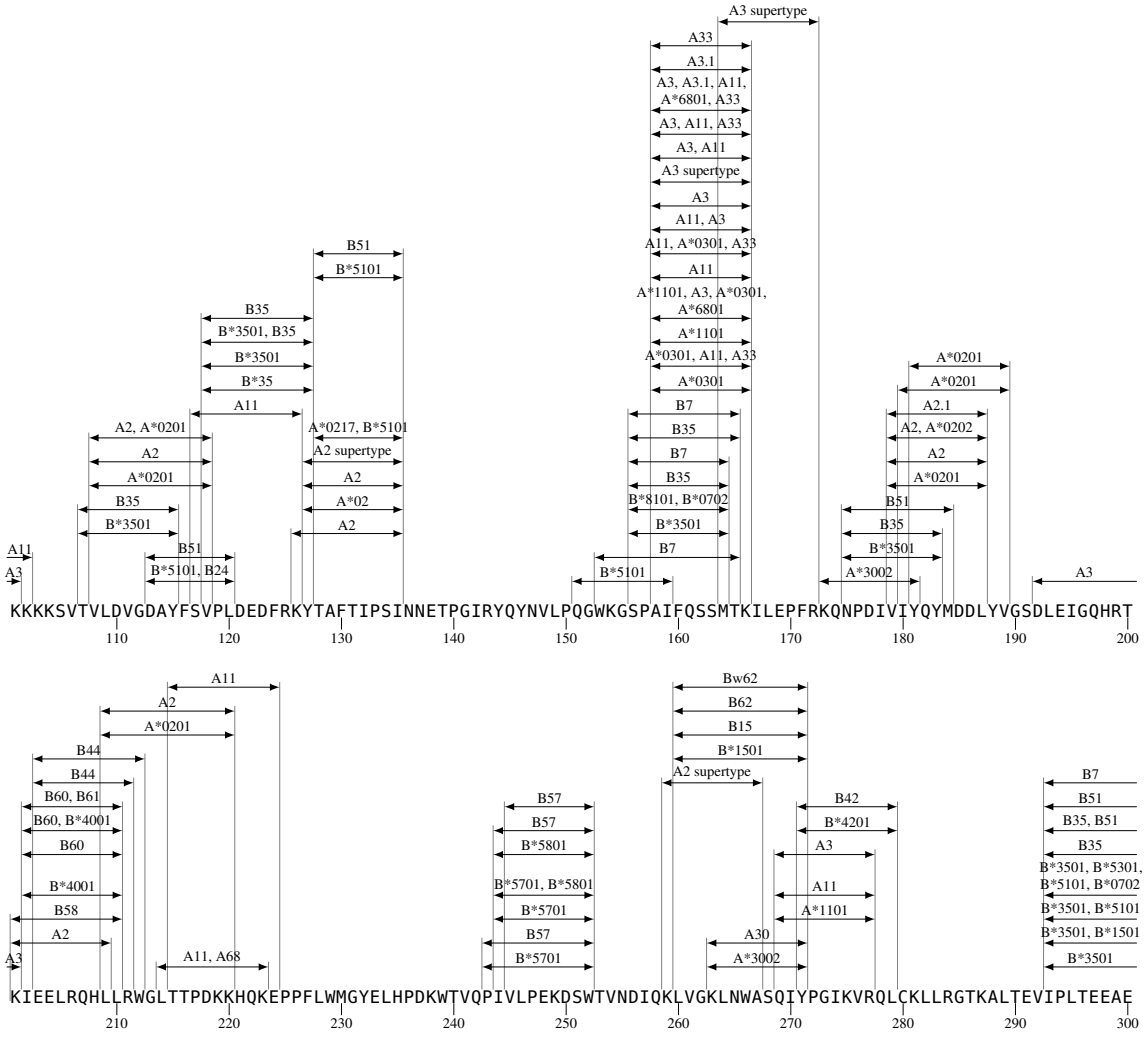
II-C-4 Gag/Pol TF CTL, CD8+, Epitope Map

II-C-5 Protease CTL, CD8+, Epitope Map



II-C-6 RT CTL, CD8+, Epitope Map




A3 supertype
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A11
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B35
B7
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110 120 130 140 150 160 170 180 190 200
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A3
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B62
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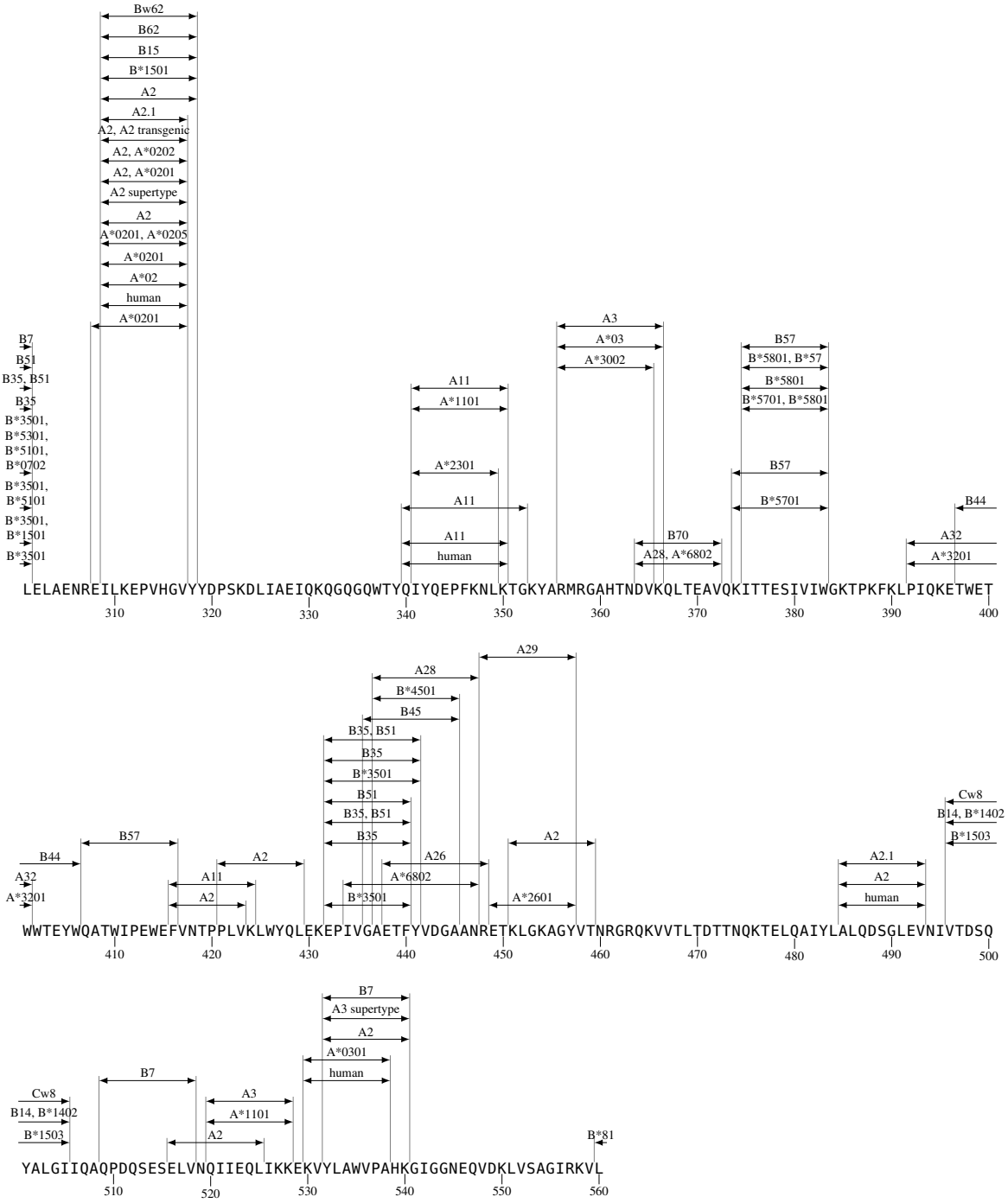
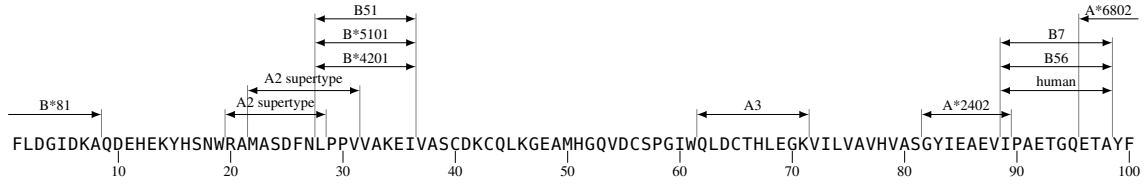
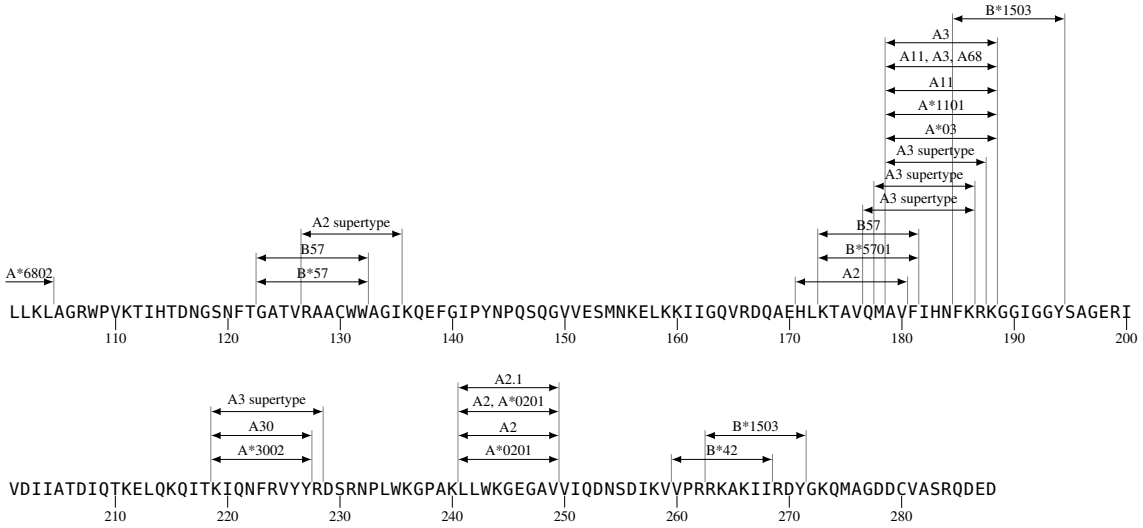
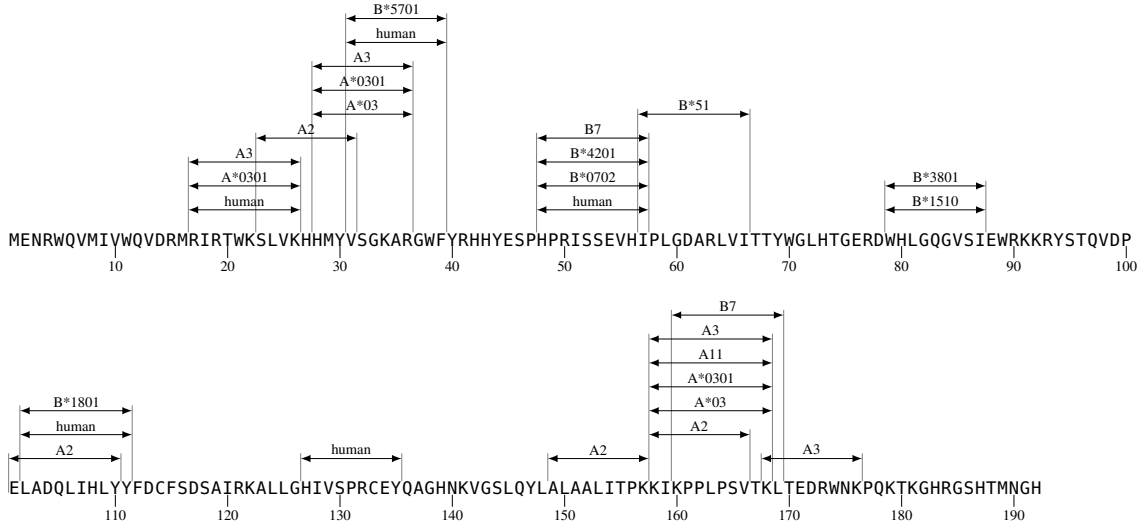


II-C-7 Integrase CTL, CD8+, Epitope Map

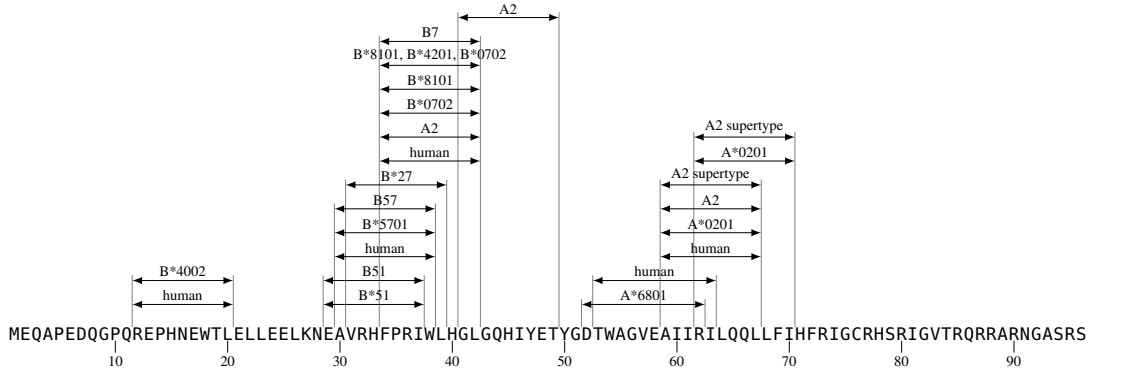




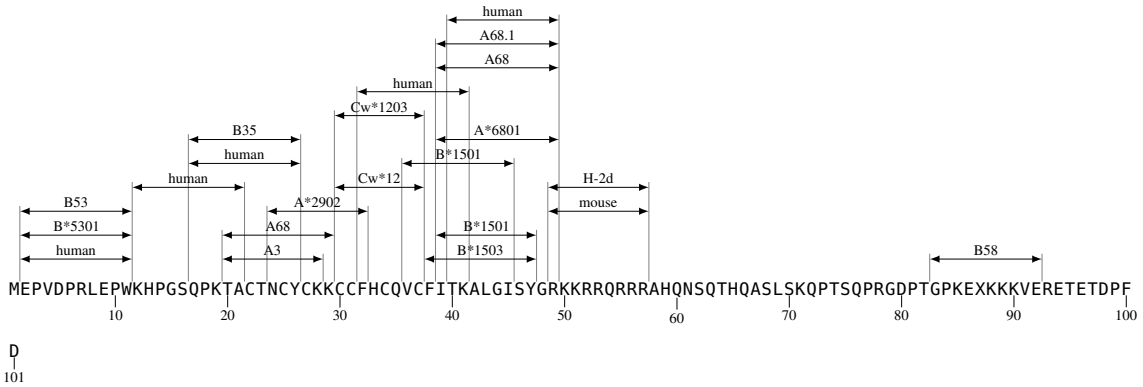
II-C-8 Vif CTL, CD8+, Epitope Map



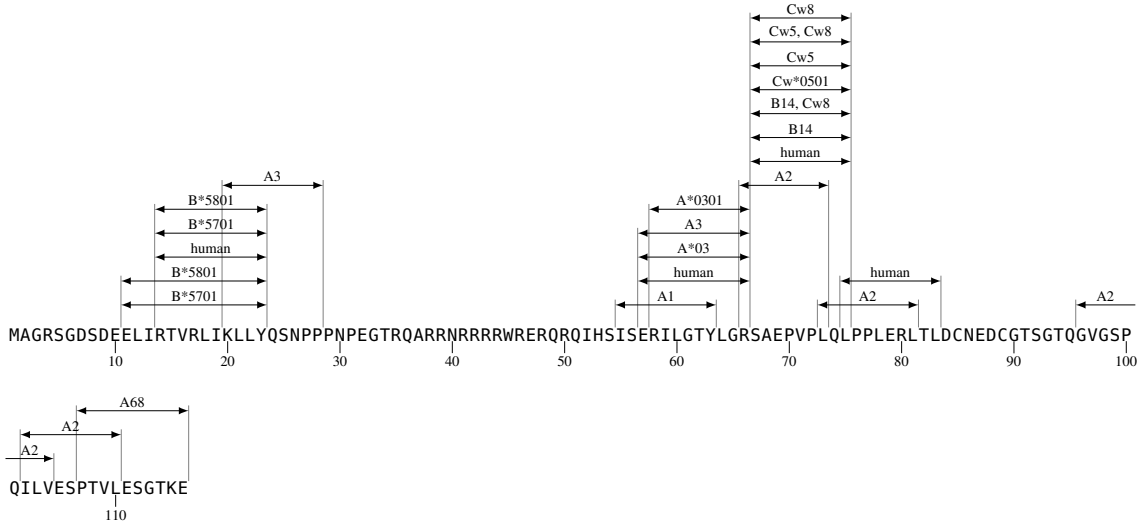
II-C-9 Vpr CTL, CD8+, Epitope Map



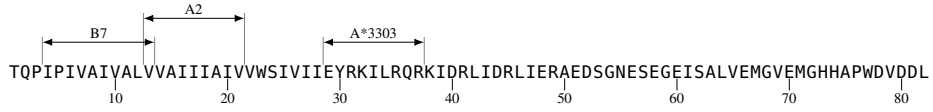
II-C-10 Tat CTL, CD8+, Epitope Map



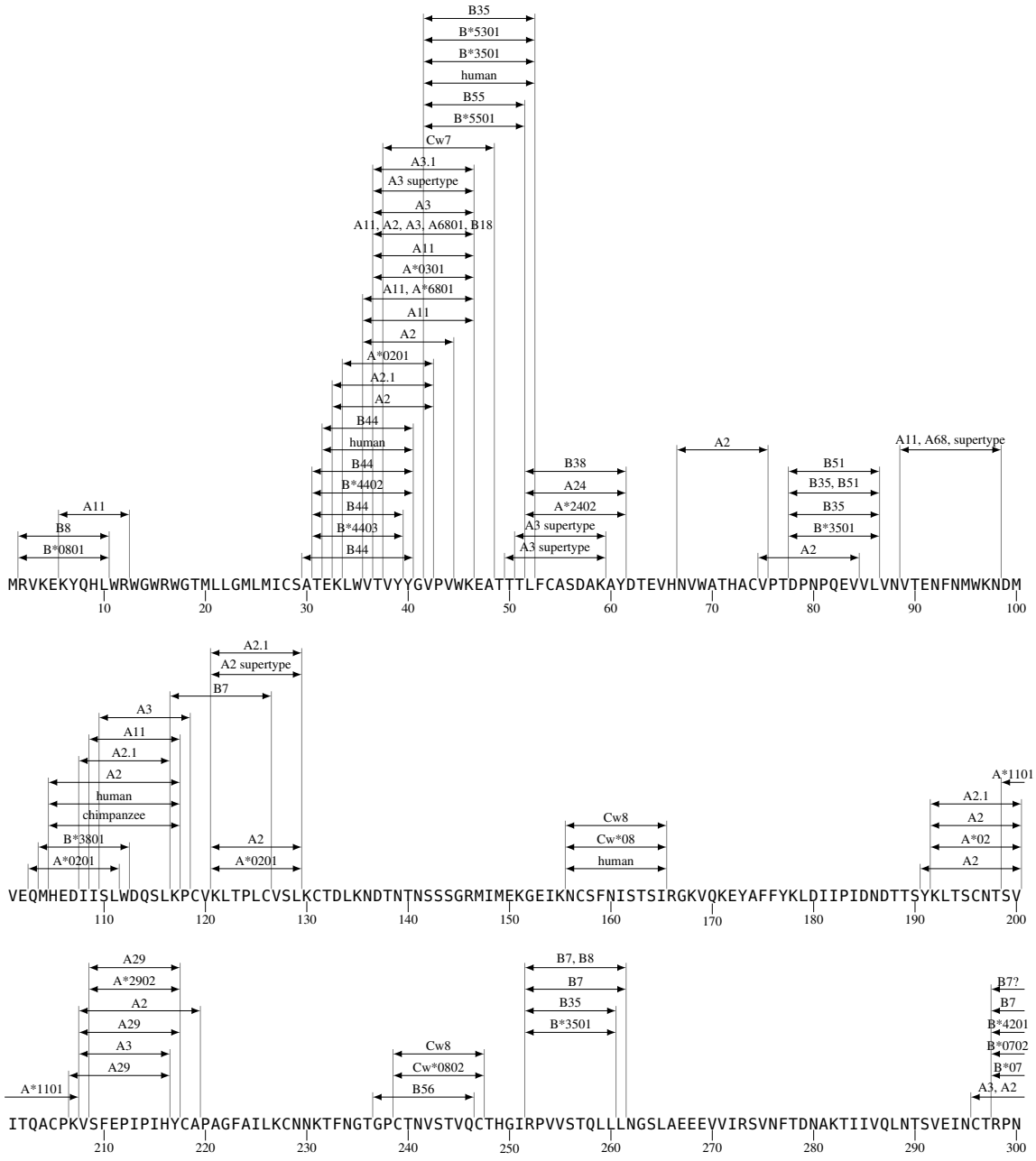
II-C-11 Rev CTL, CD8+, Epitope Map

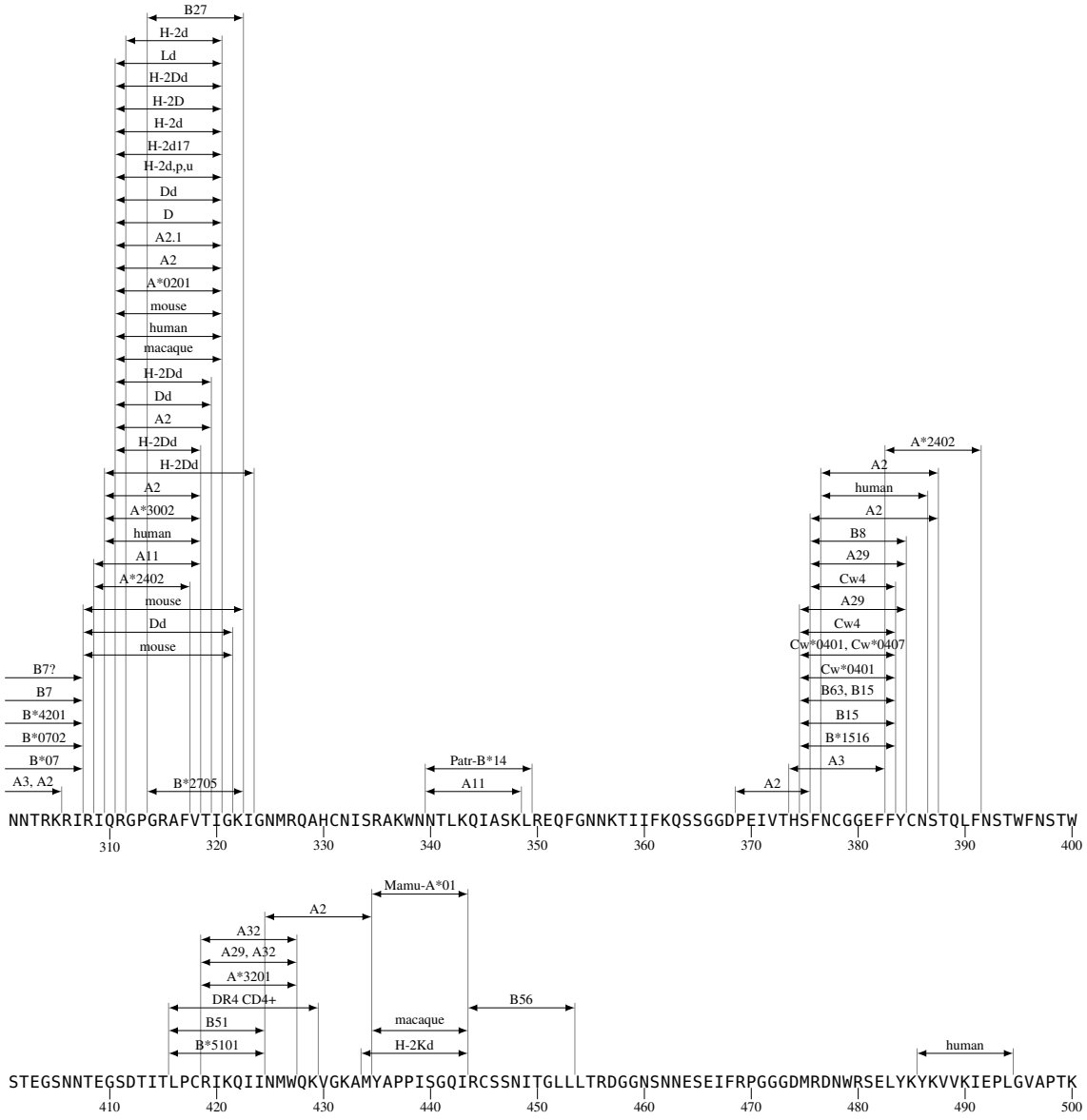


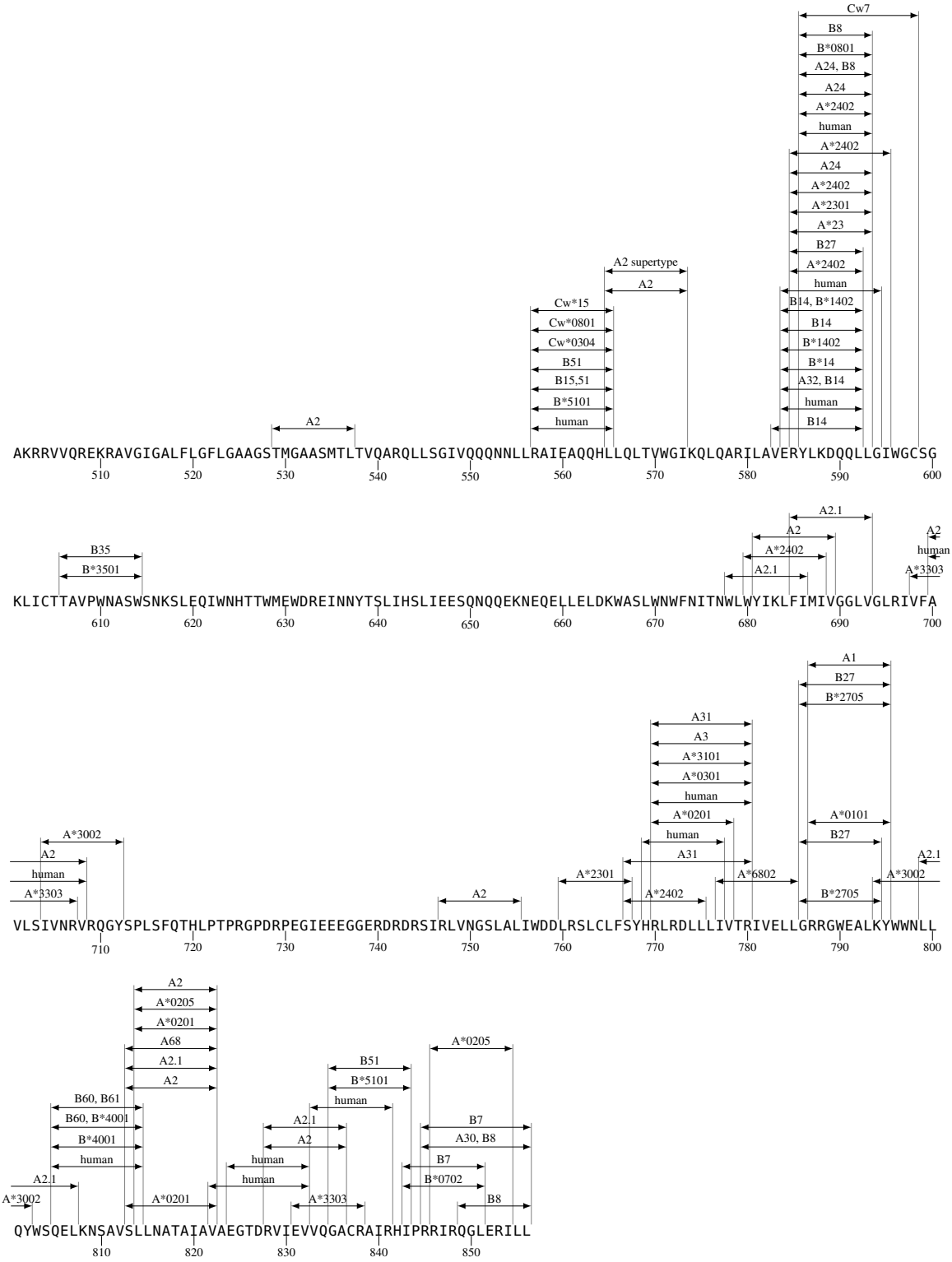
II-C-12 Vpu CTL, CD8+, Epitope Map



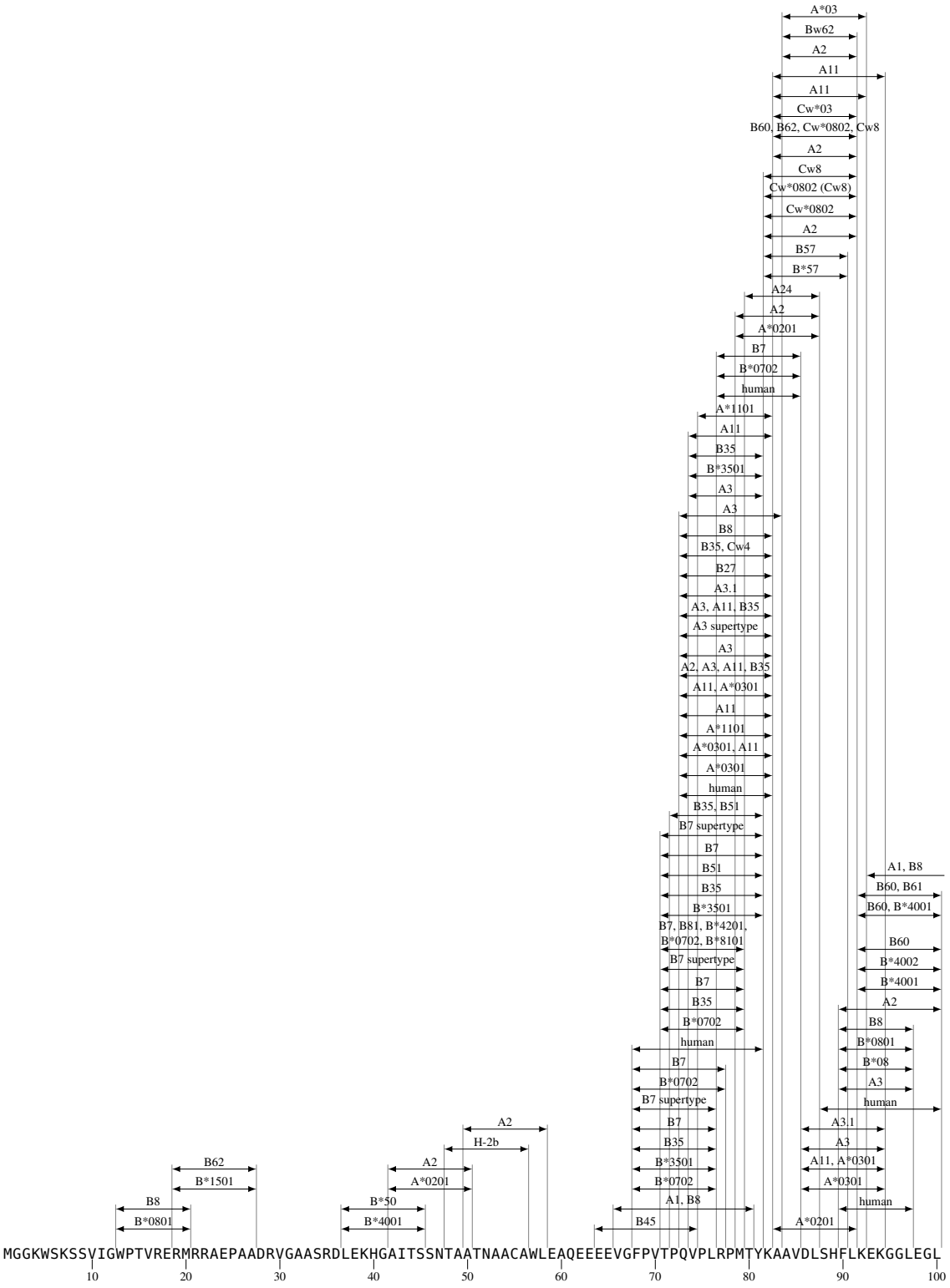
II-C-13 gp160 CTL, CD8+, Epitope Map

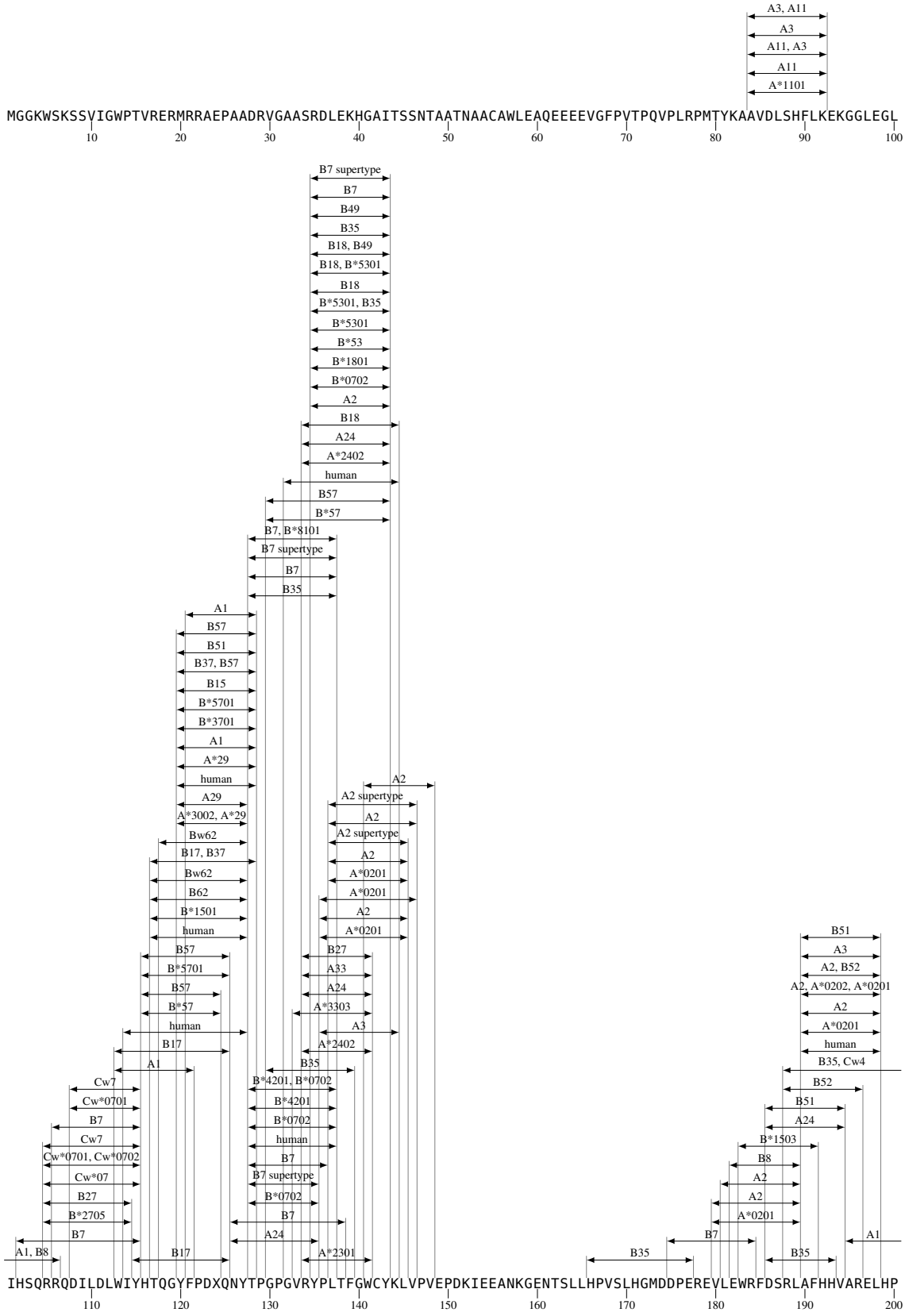


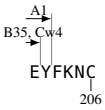

B27
H-2d
Ld
H-2Dd
H-2D
H-2d
H-2d17
H-2d,p,u
Dd
D
A2.1
A2
A*0201
mouse
human
macaque
H-2Dd
Dd
A2
H-2Dd
H-2Dd
A2
A*3002
human
A11
A*2402
mouse
Dd
mouse
B7?
B7
B*4201
B*0702
B*07
A3, A2
B*2705
Patr-B*14
A11
A*2402
A2
human
A2
B8
A29
Cw4
A29
Cw4
Cw*0401, Cw*0407
Cw*0401
B63, B15
B15
B*1516
A3
A2
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLREQFGNNKTIIFKQSSGGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTW
310
320
330
340
350
360
370
380
390
400
Mamu-A*01
A2
A32
A29, A32
A*3201
DR4 CD4+
B51
B*5101
B56
macaque
H-2Kd
human
STEGSNNTEGSDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNITGLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTK
410
420
430
440
450
460
470
480
490
500


Cw7
B8
B*0801
A24, B8
A24
A*2402
human
A*2402
A24
A*2402
A*2301
A*23
B27
A*2402
human
B14, B*1402
B14
B*1402
B*14
A32, B14
human
B14
A2 supertype
A2
Cw*15
Cw*0801
Cw*0304
B51
B15,51
B*5101
human
A2
AKRRVVQREKRAVGIGALFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
510 520 530 540 550 560 570 580 590 600
A2.1
A2
A2
human
B35
B*3501
A*2402
A2.1
A*3303
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWFNITNWLWYIKLFIMIVGGLVGLRIVFA
610 620 630 640 650 660 670 680 690 700
A1
B27
B*2705
A31
A3
A*3101
A*0301
human
A*0201
A*0101
A*3002
human
B27
A2
A31
A2.1
human
A*2301
A*6802
A*3002
A*3303
A2
A*2402
B*2705
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVNGSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
710 720 730 740 750 760 770 780 790 800
A2
A*0205
A*0201
A68
A2.1
A2
A*0205
B51
B*5101
human
B60, B61
B60, B*4001
B*4001
human
A2.1
A2
B7
A30, B8
B7
B*0702
B8
A2.1
A*3002
A*0201
human
human
A*3303
QYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQGACRAIRHIPRRIRQGLERILL
810 820 830 840 850

II-C-14 Nef CTL, CD8+, Epitope Map




A3, A11
A3
A11, A3
A11
A*1101
MGGKWSKSSVIGWPTVRERMRRAEPAADRVGAASRDLEKHGAITSSNTAATNAACAWLEAQEEEEVGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGLEGL
10 20 30 40 50 60 70 80 90 100
B7 supertype
B7
B49
B35
B18, B49
B18, B*5301
B18
B*5301, B35
B*5301
B*53
B*1801
B*0702
A2
B18
A24
A*2402
human
B57
B*57
B7, B*8101
B7 supertype
B7
B35
A1
B57
B51
B37, B57
B15
B*5701
B*3701
A1
A*29
human
A29
A*3002, A*29
Bw62
B17, B37
Bw62
B62
B*1501
human
B57
B*5701
B57
B*57
human
B17
A1
Cw7
Cw*0701
B7
Cw7
Cw*0701, Cw*0702
Cw*07
B27
B*2705
B7
A1, B8
A2
A2 supertype
A2
A2 supertype
A2
A*0201
A*0201
A2
A*0201
B27
A33
A24
A*3303
A3
A*2402
B35
B*4201, B*0702
B*4201
B*0702
human
B7
B7 supertype
B*0702
B7
A24
B17
A*2301
B51
A3
A2, B52
A2, A*0202, A*0201
A2
A*0201
human
B35, Cw4
B52
B51
A24
B*1503
B8
A2
A2
A*0201
B7
A1
B35
B35
IHSQRRQDILDLWIYHTQGYFPDXQNYTPGPGVRYPLTFGWCYKLVPVEPDKIEEANKGENTSLLHPVSLHGMDDPEREVLEWRFDSRLAFHHVARELHP
110 120 130 140 150 160 170 180 190 200


A1
B35, Cw4
EYFKNC
206

Part III

HIV Helper CD4+ T-Cell Epitopes

III-A

Summary

This part includes tables, maps, and associated references of HIV-specific helper T-cell (Th) epitopes arranged sequentially according to the location of the proteins in the HIV-1 genome. We attempted to make this part as comprehensive as possible, requiring that the epitope be contained within a defined region of a maximum of 30 amino acids, but not that the optimal boundaries be defined. Studies that were based on the analysis of whole proteins are described at the end of each protein section. The same epitope can have multiple entries, as each entry represents a single publication in this part of the database. HLA specificity is usually not determined for Th epitopes. For more recent updates, epitope sequence alignments, and useful search capabilities, please see our web site: `http://www.hiv.lanl.gov/content/immunology`. Helper T-cell responses to proteins with no defined epitopes are listed at the end of each protein section.

Recent studies utilize multiple functions attributed to T cells to define responses, and the simple distinctions of cytotoxic T-cell and helper T-cells have become blurred as more is learned about the range of responses triggered in CD4 and CD8 positive T-cells responding to antigenic stimulus. When adding the most recent studies to the database, we have tried to place T cell responses in a reasonable manner into our traditional helper T cell and CTL parts, and to specify the assay used to measure the response in each study.

III-A-1 Epitope tables

Each T-helper epitope has a multi-part basic entry:

HXB2 location: The viral strain HXB2 (GenBank Accession Number K03455) is used as a reference strain throughout this publication. The position of the defined epitope location relative to the sequence of the HXB2 protein is indicated. The numbering in this table corresponds to the protein maps. Because of HIV-1 variation the epitope may not actually be present in HXB2; rather, the position in HXB2 indicates the position aligned to the epitope. HXB2 was selected as the reference strain because so many studies use HXB2, and because crystal structures for HXB2-related proteins are often available. The precise positions of an epitope on the HXB2 reference strain can be readily obtained using the interactive position locator at our web site: `http://www.hiv.lanl.gov/content/hiv-db/LOCATE/locate.html`.

Author location: The amino acid positions of the epitope boundaries and the reference sequence are listed as given in the primary publication. Frequently, these positions as published are imprecise, and do not truly correspond to the numbering of the sequence, but they provide a reasonable guide to the peptide's approximate location in the protein. Also, in many cases the reference sequence identification was not provided, and in such cases it is not possible to use these numbers to specify precise locations.

Epitope: The amino acid sequence of the epitope of interest as defined in the reference, based on the reference strain used in the study defining the epitope. On occasions when only the position numbers and not the actual peptide sequence were specified in the original publication, we tried to fill in the peptide sequence based on the position numbers and reference strain. If the sequences were numbered inaccurately by the primary authors, or if we made a mistake in this process, we may have misrepresented the binding site's amino acid sequence. Because of this uncertainty, epitopes that were not explicitly written in the primary publication, that we determined by looking up the reference strain and the numbered location, are followed by a question mark in the table.

Epitope name: If the epitope has a name attributed by the publication, it is recorded here, e.g. "SL9".

Subtype: The subtype under study, generally not specified for B subtype.

Immunogen: The antigenic stimulus of the Th response. Often this is an HIV-1 infection. If a vaccine was used as the original antigenic stimulation, not a natural infection, this is noted separately, and additional information about the vaccine antigen is provided as available.

Species (MHC): The species responding and MHC or HLA specificity of the epitope.

Donor MHC: The HLA genotype of the individual that responded to the epitope.

Country: The country where the samples were obtained—generally not specified if the study was conducted in the United States.

Assay type: Assay used to characterize the response.

Keywords: Keywords are a searchable field for the web interface that is included in the T-cell sections of the printed version to help identify entries of particular interest.

Reference: The primary reference (sometimes two or more directly related studies are included). Details for some of the earlier references are in Part V.

Following the entry for a given Th epitope brief comments explain the context in which the epitope was studied and what was learned about the epitope in a given study.

III-A-2 HIV protein epitope maps

All HIV Th epitopes mapped to within a region of 18 amino acids or less are indicated on the HIV protein epitope maps. The location and HLA restriction elements of Th epitopes are indicated on protein sequences of HXB2. These maps are meant to provide the relative location of defined epitopes on a given protein, but the HXB2 sequence may not actually carry the epitope of interest, as it may vary relative to the sequence for which the epitope was defined. Epitopes with identical boundaries and HLA fields are included in the maps only once. If one laboratory determines HLA presenting molecules at the serotype level (example: A2) and another at the genotype level (example: A*0201) both will be included in the map. MHC specificities are indicative of the host species; when no MHC presenting molecule is defined, the host species is noted.

III-A-3 Alignments

To conserve space, no epitope alignments are provided in this book, but they can be generated using the Th epitope search tool at `http://www.hiv.lanl.gov/content/immunology`. All epitopes are aligned to the HXB2 sequence, with the sequence used to define the epitope indicated directly above it. Sequences are sorted by their subtype and country of origin.

The master alignment files from which the epitope alignments were created are available at our web site[1]. The alignments were modified in some cases to optimize the alignment relative to the defined epitope and minimize insertions and deletions; epitope alignments are generated by anchoring on the C-terminal residue. A dash indicates identity to the consensus sequence, and a period indicates an insertion made to maintain the alignment. Stop codons are indicated with a `$`, and frameshifts by a `#`, or ambiguous codons (nucleotide was `r`, `y`, or `n`) by an `x`; they are inserted to maintain the alignments. In consensus sequences an upper case letter indicates the amino acid was present in all sequences, a lower case letter indicates the amino acid was present in most sequences in a given position, and a question mark indicates two or more amino acids were represented with equal frequency.

[1] `http://www.hiv.lanl.gov/content/hiv-db/ALIGN_CURRENT/ALIGN-INDEX.html`

III-B

HIV Helper T-Cell Epitope Tables

All HIV Helper T-Cell epitopes are arranged by protein position. The table entries are sorted in a nested way—first by protein, then by HXB2 start location within the protein and finally by HLA presenting molecule. Epitopes for which the HXB2 location is unknown appear at the end of the listing of the protein in which they are located.

III-B-1 Gag p17 Helper, CD4+, T-cell epitopes

HXB2 Location p17 (1–18)
Author Location p17 (1–18 B consensus)
Epitope MGARASVLSGGELDRWEK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This epitope was recognized by 14% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p17 (9–26)
Author Location p17 (9–26 B consensus)
Epitope SGGELDRWEKIRLRPGGK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 22% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p17 (17–34)
Author Location p17 (17–34 B consensus)
Epitope EKIRLRPGGKKKYKLKHI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 14% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.

- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p17 (18–42)
Author Location p17 (18–42 PV22)
Epitope KIRLRPGGKKKYKLKHIVWASRELE
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*13)
Donor MHC A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13
Keywords HAART, ART, Th1, Th2
References Lotti *et al.* 2002

- 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response.
- For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity.
- 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 6 recognized this peptide sequence restricted by DRB1*13. This clone had a high SI (27.1 to p55, 90.6 to peptide) secreted IFNgamma, indicative of a Th1 response, as well as TNFalpha. Clone 6 was highly cytotoxic, through a perforin-mediated pathway.

HXB2 Location p17 (21–35)
Author Location p17 (21–35 SF2)
Epitope LRPGGKKKYKLKHIV
Immunogen HIV-1 infection
Species (MHC) human (DR13.02)
Keywords escape
References Harcourt *et al.* 1998

- 43 asymptomatic HIV+ individuals were screened for proliferative responses to HIV – 12 showed a response, and dominant epitopes were mapped for two individuals, one in p24 and one in p17.
- Patient 024's naturally occurring variant LRPGGKKKYQLKHIV also elicited a strong proliferative response.
- Naturally occurring variants of this epitope were found within the individual who made this response – several did not stimulate the CD4+ T-cell line that recognized the index peptide, suggestive of immune escape.

HXB2 Location p17 (22–29)
Author Location p17 (22–29 LAI)
Epitope RPGGKKKY?
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.
- Schrier lists this peptide as p24(22-29), but it appears to be in p17.

HXB2 Location p17 (32–46)
Author Location p17 (32–46 B Consensus)
Epitope KHIVWASRELERFAV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p17 (33–47)
Author Location p17 (33–47 IIIB, B10)
Epitope HIVWASRELERFAVN?
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- Peptides were identified that commonly evoke T-cell responses – 57% of 90 HIV+ people had a T-cell response to this peptide.

HXB2 Location p17 (35–59)
Author Location p17 (35–49 PV22)
Epitope VWASRELERFAVNPGLLETSEGCRQ
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*13)
Donor MHC A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13
Keywords HAART, ART, Th1, Th2, TCR usage
References Lotti *et al.* 2002

- 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response.
- For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity.
- 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 25 recognized this peptide sequence restricted by DRB1*13 using TCR Vβ 5.1. This clone had a SI of 4.9 to p55, 13.7 to peptide, secreted low levels of IFNgamma, indicative of a Th1 response. Clone 25 had cytotoxic activity, mediated through both a perforin and a Fas-based pathway.

HXB2 Location p17 (37–51)
Author Location p17 (37–51 B consensus)
Epitope ASRELERFAVNPGLL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB*0101, DRB1*0401, DRB1*0405, DRB1*0701, DRB1*1302, DRB1*1501)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This peptide was recognized by 36% of the study group.
- The peptides that were recognzied by the most people were able to bind broadly to multiple HLA-DR molecules. This peptide showed high cross-reactive binding capacity and bound to 6/8 tested common HLA-DR molecules.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p17 (39–47)
Author Location p17 (B consensus)
Epitope RELERFAVN
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*1302)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), immunodominance
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This epitope was in the overlap between two highly reactive peptides, and was fine mapped and found to be presented by DRB*1302.

HXB2 Location p17 (41–51)
Author Location p17 (41–51 B consensus)
Epitope LERFAVNPGLL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*1302)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This core epitope, LERFAVNPGLL,was found to bind to 1/8 HLA-DR proteins tested, DRB*1302.

HXB2 Location p17 (42–51)
Author Location p17 (B consensus)
Epitope ERFAVNPGLL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB3*0202, DRB3*0301)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding

Keywords supervised treatment interruptions (STI), immunodominance
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This epitope was in the overlap between two highly reactive peptides, and was fine mapped and two different presenting alleles for two different clones were determined, and found to be DRB3*0202, DRB3*0301

HXB2 Location p17 (42–58)
Author Location p17 (42–58 B consensus)
Epitope ERFAVNPGLLETSEGCR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DRB1*0405, DRB1*1101, DRB1*1302)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), immunodominance
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 28% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The peptides that were recognzied by the most people were able to bind broadly to multiple HLA-DR molecules. This peptide showed high cross-reactive binding capacity and bound to 4/8 tested HLA-DR molecules.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p17 (70–86)
Author Location p17 (70–86 B Consensus)
Epitope TGSEELRSLNTVALY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p17 (77–94)
Author Location p17 (77–94 B consensus)
Epitope SLYNTVATLYCVHQRIEV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DRB1*0401, DRB1*0405, DRB1*0701, DRB1*1302, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This peptide was recognized by 25% of the study group.
- The peptides that were recognzied by the most people were able to bind broadly to multiple HLA-DR molecules. This peptide showed high cross-reactive binding capacity and bound to 6/8 tested common HLA-DR molecules.

- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p17 (93–107)
Author Location p17 (93–107 IIIB, B10)
Epitope EIKDTKEALDKIEEE
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location p17 (118–132)
Author Location p17 (118–132 IIIB, B10)
Epitope AAADTGHSSQVSQNY
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

III-B-2 Gag p24 Helper, CD4+, T-cell epitopes

HXB2 Location p24 (1–9)
Author Location p24 (133–141 HXB2)
Epitope PIVQNIQGQ
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords HAART, ART
References Boritz *et al.* 2003

- HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were also recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.
- The TCR that recognized this epitope used Vβ5.1.

HXB2 Location p24 (1–11)
Author Location p24 (1–11 SF2)
Epitope PIVQNLQGQMV
Immunogen HIV-1 infection
Species (MHC) human (DR1)
Keywords escape
References Harcourt *et al.* 1998

- 43 asymptomatic HIV+ individuals were screened for proliferative responses to HIV – 12 showed a response, and dominant epitopes were mapped for two individuals, one in p24 and one in p17.
- Out of five truncated versions of peptide PIVQNLQGQMVHQAISPRTL, only p24(1-11) elicited a proliferative response.
- Nine naturally occurring variants of this epitope were found within the individual who made this response – all bound to HLA-DR1, but three did not stimulate the CD4+ T-cell line that recognized the index peptide, suggestive of immune escape.

HXB2 Location p24 (1–15)
Author Location p24 (133–147 IIIB, B10)
Epitope PIVQNIQGQMVHQAI
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- Peptides were identified that commonly evoke T-cell responses – 62% of 90 HIV+ people had a T-cell response to this peptide.

HXB2 Location p24 (1–22)
Author Location p24 (133–154 SF2)
Epitope PIVQNIQGQMVHQAISPRTLNA
Immunogen HIV-1 infection
Species (MHC) human
References Rosenberg *et al.* 1997

- While anti-HIV CD4 Th responses are characteristically undetectable in chronic infections, strong p24-specific proliferative responses were inversely correlated with low viral load in 10 chronically infected people.
- The dominant proliferative response in one of two long term survivors was to this peptide.

HXB2 Location p24 (7–21)
Author Location Gag (171–185)
Epitope QGQMVHQAISPRTLN
Epitope name Gag 171
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds to nine HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRBI*0405, DRB1*1302, DRB1*0701, DRB1*0901, DRB5*0101 and DRB4*0101 with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 52% of clade B isolates.
- 7/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location p24 (7–21)

Author Location p24 (171–185)
Epitope QGQMVHQAISPRTLN
Epitope name Gag1
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Country United Kingdom.
Assay type proliferation, Intracellular cytokine staining
Keywords supertype, rate of progression
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.
- Gag1 was 1 of 3 peptides that had a negative correlation between absolute number of responding cells and viral load.

HXB2 Location p24 (7–21)
Author Location Gag (171–185)
Epitope QGQMVHQAISPRTLN
Epitope name Gag 171
Immunogen Vaccine
Vector/Type: DNA with CMV promotor, peptide *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (I-Ab and HLA-DR)
Donor MHC H-2b
Keywords vaccine-specific epitope characteristics, immunodominance
References Livingston *et al.* 2002

- Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice.
- Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.

HXB2 Location p24 (9–26)
Author Location p24 (9–26 B Consensus)
Epitope QMVHQAISPRTLNAWVKV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p24 (11–26)
Author Location p24 (143–157)
Epitope VHQAISPRTLNAWVKC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.
- Matches 3/3 anchor residues for HLA DR: **V**HQAI**S**PR**T**

HXB2 Location p24 (11–30)
Author Location Gag (143–152 SF2)
Epitope VHQAISPRTLNAWVKVVEEK
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade SF2 *HIV component:* p24 Gag
Species (MHC) mouse (H-2^d, H-2^b)
Keywords immunodominance, Th1
References Mata & Paterson 1999

- Listeria moncytogenes is an intracellular bacterium that lives in the cytoplasm and generates a cell-mediated immune response.
- Listeria moncytogenes vaccine expressing HIV-1 p24 protein (Lm-Gag) was used to stimulate gag specific CD4+ T cell proliferative responses in BALB/c(H-2d) and C57BL/6(H-2b) mice.
- Two of three reactive p24 peptides (out of 22 overlapping peptides that span p24) were recognized by both murine strains – this epitope is immunodominant in C57BL/6 mice and also can stimulate a BALB/c response.
- The proliferative response is due to CD4+, IFNγ producing cells, a Th1 response.

HXB2 Location p24 (11–30)

Author Location p24 (143–162 HXB2)
Epitope VHQAISPRTLNAWVKVVEEK
Subtype B
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2^d, H-2^b)
References Mata & Paterson 1999

- BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.
- The class II T helper response was probed using 20 mer peptides that overlapped by 10, and the peptides VHQAISPRTLNAWVKVVEEK and FRDYVDRFYKTLRAEQASQD were recognized in H-2^b and H-2^d mice.

HXB2 Location p24 (21–36)
Author Location p24 (153–167)
Epitope NAWVKVVEEKAFSPEC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.

HXB2 Location p24 (23–40)
Author Location p24 (23–40 B Consensus)
Epitope WVKVVEEKAFSPEVIPMF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p24 (28–36)
Author Location p24 (160–168 HXB2)
Epitope EEKAFSPEV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords HAART, ART
References Boritz *et al.* 2003

- HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were also recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.
- The TCR that recognized this epitope used Vβ2.

HXB2 Location p24 (28–38)
Author Location p24 (HXB2)
Epitope EEKAFSPEVIP
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DQ5)
Assay type CD4 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine antigen design
References SenGupta *et al.* 2004

- Multiple HLA calss I-restricted and class II-restricted T-cell epitopes were shown to be processed and presented from an exogenously added HIV-1 gag-p24 peptide complexed to a heat shock protein. T-cell recognition of the complex was shown to be inhibited by brefeldin A indicating an endoplasmic reticulum-dependent pathway.

HXB2 Location p24 (28–38)
Author Location p24 (161–171 NY-5)
Epitope EEKAFSPEVIP
Epitope name EP11
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DQ5)
Donor MHC DR11, DR14, Drw52, DQ3, DQ5
Country United States.
Assay type proliferation, CD4 T-cell Elispot - IFNγ, Chromium-release assay
Keywords inter-clade comparisons, rate of progression, acute infection, early treatment, variant cross-recognition or cross-neutralization
References Norris *et al.* 2004

- Five CD4-T cell epitopes in Gag-p24 were studied, and a minimum epitope length of 6-16 amino acids were found to be required for CD4+ T cell proliferation. Cross-clade recognition was studied and found to be impaired in 17/32 variants tested.
- Patient AC-01, who was infected with HIV-1 in 1997, recognized this epitope and epitope EPRGSDIAGT during acute infection, and 19 months post-initiation of ART therapy started during primary infection.
- The epitope EEKAFSPEVIP is highly conserved in the B clade. Common variants from other clades were tested and all markedly diminished responses, including eeRafspevip, eekaLspevip, and eDkafspevip (all found in clade A); eekGfspevip, eekGfNpevip (clades A and CRF01_AE); eekafspeIip (clade C); eekafNpevip (clade D).
- Minimum length peptides for the epitopes studies were not particularly optimal, and peptides longer than the minimum, up to 22 amino acids, were often as potent, in marked contrast to CD8+ T cell responses.

HXB2 Location p24 (31–46)
Author Location p24 (163–177)
Epitope AFSPEVIPMFSALSEC
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
References Bedford *et al.* 1997

- E elicits a primary proliferative response in PBMC from uninfected donors.
- Peptide contains a CTL epitope identified in HIV-positive patients.
- Peptide binds to HLA A*0201 and causes regulation of class I expression on T2 cells.
- Matches 3/3 anchor residues for HLA DR: **V**IPMF**S**AL**S**

HXB2 Location p24 (31–47)
Author Location p24 (31–47 B Consensus)
Epitope AFSPEVIPMFSALSEGA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p24 (31–52)
Author Location p24 (163–184 SF2)
Epitope AFSPEVIPMFSALSEGATPQDL
Immunogen HIV-1 infection
Species (MHC) human
References Rosenberg *et al.* 1997

- Low viral load correlated with strong HIV-1-specific proliferative response.
- A proliferative response to this epitope was detected in two long term survivors.

HXB2 Location p24 (34–49)
Author Location p24 (HXB2)
Epitope PEVIPMFSALSEGATP
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DR1)
Assay type CD4 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine antigen design, characterizing CD8+ T cell responses
References SenGupta *et al.* 2004

- Multiple HLA class I-restricted and class II-restricted T-cell epitopes were shown to be processed and presented from an exogenously added HIV-1 gag-p24 peptide complexed to a heat shock protein. T-cell recognition of the complex was shown to be inhibited by brefeldin A indicating an endoplasmic reticulum-dependent pathway.

HXB2 Location p24 (34–49)
Author Location p24 (168–177 NY-5)
Epitope PEVIPMFSALSEGATP
Epitope name PP16
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DR1)
Donor MHC DR1, DR11, DRw52, DQ5, DQ7
Country United States.
Assay type proliferation, CD4 T-cell Elispot - IFNγ, Chromium-release assay
Keywords rate of progression, acute infection, early treatment, variant cross-recognition or cross-neutralization
References Norris *et al.* 2004

- Five CD4-T cell epitopes in Gag-p24 were studied, and a minimum epitope length of 6-16 amino acids were found to be required for CD4+ T cell proliferation. Cross-clade recognition was studied and found to be impaired in 17/32 variants tested.
- Patient AC-25 was an acute seroconvertor at the time of sampling, infected with HIV-1 in 1998, and given ARVs during primary infection. The study subject was resampled 18 months after initiation of therapy.

- Natural variants of the epitope PEVIPMFSALSEGATP diminished the level of the response, including pevipmfPalsegStp and pevipmfsalsegStp, found in CRF01 AE; peIipmfTalsegatp, clade C; pevipmfsalSegatp, clade B; pevipmfTalsegatp, clades A, B and C; and pevipVfsalsegatp, clade A.
- Minimum length peptides for the epitopes studies were not particularly optimal, and peptides longer than the minimum, up to 22 amino acids, were often as potent, in marked contrast to CD8+ T cell responses.

HXB2 Location p24 (35–44)
Author Location p24 (167–176 HXB2)
Epitope EVIPMFSALS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords HAART, ART
References Boritz *et al.* 2003

- HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were also recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.

HXB2 Location p24 (35–44)
Author Location p24 (HXB2)
Epitope EVIPMFSALS
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DR4)
Assay type CD4 T-cell Elispot - IFNγ
Keywords epitope processing, vaccine antigen design, characterizing CD8+ T cell responses
References SenGupta *et al.* 2004

- Multiple HLA calss I-restricted and class II-restricted T-cell epitopes were shown to be processed and presented from an exogenously added HIV-1 gag-p24 peptide complexed to a heat shock protein. T-cell recognition of the complex was shown to be inhibited by brefeldin A indicating an endoplasmic reticulum-dependent pathway.

HXB2 Location p24 (35–44)
Author Location p24 (168–177 NY-5)
Epitope EVIPMFSALS
Epitope name ES10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DR4)
Donor MHC DR4, DR15, DRw51, DRw53, DQ3, DQ6
Country United States.
Assay type proliferation, CD4 T-cell Elispot - IFNγ, Chromium-release assay
Keywords rate of progression, acute infection, early treatment, variant cross-recognition or cross-neutralization
References Norris *et al.* 2004

- Five CD4-T cell epitopes in Gag-p24 were studied, and a minimum epitope length of 6-16 amino acids were found to be required for CD4+ T cell proliferation. Cross-clade recognition was studied and found to be impaired in 17/32 variants tested.
- Patient 161J, was infected with HIV-1 in the mid 1980s was one of the two LTNPs examined in this study. 161J was ART naive.
- Natural variants of the epitope EVIPMFSALS gave diminished responses including evipmfTals, common in clades A, B and C; and evipVfsals, clade A; evipmfsalA, a clade B variant; and eIipmfTals, clade C. The exception was the CRF01 AE variant evipmfPals which was as reactive as the original peptide tested.
- Minimum length peptides for the epitopes studies were not particularly optimal, and peptides longer than the minimum, up to 22 amino acids, were often as potent, in marked contrast to CD8+ T cell responses.

HXB2 Location p24 (41–56)
Author Location p24 (173–187)
Epitope SALSEGATPQDLNTMC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.

HXB2 Location p24 (48–62)
Author Location p24 (180–194)
Epitope TPQDLNTMLNTVGGH
Immunogen HIV-1 infection
Species (MHC) human
References Adams *et al.* 1997

- One of four immunogenic Gag peptides used in study of proliferative response to p24.
- Homology to an SIV epitope recognized by macaque T-cells.
- T-cells from 8 of 19 HIV+ individuals responded to this epitope.
- Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response.

HXB2 Location p24 (51–66)
Author Location p24 (183–197)
Epitope DLNTMLNTYGGHQAAC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.

HXB2 Location p24 (51–82)
Author Location Gag (183–214 LAI)
Epitope DLNTMLNTVGGHQAAMQMLKETINEEAAEWDR
Subtype B
Immunogen Vaccine

Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 2/10 reacted to this peptide.
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual.
- None of the 12 tested had an IgG response to this peptide.

HXB2 Location p24 (69–88)
Author Location p24 (201–220 IIIB)
Epitope LKETINEEAAEWDRVHPVHA
Epitope name P21
Immunogen in vitro stimulation or selection
Species (MHC) human (DR)
Donor MHC DR4, DR7 DQ2 and DQ3
Keywords immunodominance, Th1, Th2, TCR usage
References Venturini *et al.* 2002

- PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA class II DR restricted.
- Clone 85 recognized this peptide using TCR Vβ 8 and 18; the two TCR receptors indicates this limiting dilution represents a mixed population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.

HXB2 Location p24 (71–86)
Author Location p24 (203–220)
Epitope ETINEEAAEWDRVHPC
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.

HXB2 Location p24 (71–88)
Author Location p24
Epitope ETINEEAAEWDRVHPVHA
Epitope name 17
Subtype B
Immunogen
Species (MHC) (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
References

HXB2 Location p24 (71–88)
Author Location (203–220)
Epitope ETINEEAAEWDRVHPVHA
Subtype B
Immunogen
Species (MHC) human (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
References

HXB2 Location p24 (71–88)
Author Location
Epitope ETINEEAAEWDRVHPVHA
Epitope name 17
Subtype B
Immunogen
Species (MHC) (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
References

HXB2 Location p24 (71–88)
Author Location p24 (203–220 HXB2)
Epitope ETINEEAAEWDRVHPVHA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords HAART, ART
References Boritz *et al.* 2003

- HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells/ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.
- The Th clone that recognized this epitope utilized TCR Vβ17.

HXB2 Location p24 (71–92)
Author Location p24 (203–224 HXB2)
Epitope ETINEEAAEWDRVHPVHAGPIA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords HAART, ART
References Boritz *et al.* 2003

- HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells/ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays

based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.

HXB2 Location p24 (73–97)
Author Location p24 (205–229 PV22)
Epitope INEEAAEWDRVHPVHAGPIAPGQMR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*03)
Donor MHC A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13
Keywords HAART, ART, Th1, Th2, TCR usage
References Lotti *et al.* 2002

- 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response.
- For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity.
- 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 12 recognized this peptide sequence restricted by DRB1*03 using TCR Vβ 22. This clone had a SI of 12.4 to p55, 49.6 to peptide, secreted low levels of IFNgamma, indicative of a Th1 response. Clone 12 had cytotoxic activity, mediated through both a perforin and a Fas-based pathway.

HXB2 Location p24 (76–85)
Author Location p24 (208–217)
Epitope EAAEWDRVHP
Immunogen HIV-1 infection
Species (MHC) human
References Adams *et al.* 1997

- One of four immunogenic Gag peptides used in study of the proliferative response to p24.
- T-cells from 11 of 24 HIV+ individuals responded to this epitope.
- Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response.

HXB2 Location p24 (76–90)
Author Location p24 (208–222 IIIB, B10)
Epitope EAAEWDRVHPVHAGP
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location p24 (79–88)
Author Location p24 (211–220 HXB2)
Epitope EWDRVHPVHA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords HAART, ART
References Boritz *et al.* 2003

- HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were also recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects. Two clones recognized this epitope.

HXB2 Location p24 (81–95)
Author Location p24 (215–229 SF2)
Epitope DRVHPVHAGPIAPGQ
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* B clade SF2 *HIV component:* p24 Gag
Species (MHC) macaque
References Mills *et al.* 1990

- Responses to 3 T-cell and multiple linear B-cell epitopes were found in vaccinated macaques.

HXB2 Location p24 (81–102)
Author Location p24 (213–234 SF2)
Epitope DRVHPVHAGPIAPGQMREPRGS
Immunogen HIV-1 infection
Species (MHC) human
References Rosenberg *et al.* 1997

- While anti-HIV CD4 Th responses are characteristically undetectable in chronic infections, strong p24-specific proliferative responses were inversely correlated with low viral load in 10 chronically infected people.
- The dominant proliferative response in one of two long term survivors was to this peptide.

HXB2 Location p24 (86–94)
Author Location p24 (NY5)
Epitope VHAGPIAPG
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DQ7)
Keywords HAART, ART, supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection, cross-presentation by different HLA, early treatment, TCR usage
References Norris *et al.* 2001

- Gag-specific CD4+ helper T-cell clones were derived from one long-term non-progressor (LTNP) (CTS-01), and three individuals given therapy during acute infection, two before (AC-01 and AC-36) and one after (AC-25) STI. Gag peptide recognition induced proliferation, IFNgamma production and perforin-mediated cytotoxicity in all CD4+ T-cell clones isolated.
- 3/23 p24-derived peptides tested induced proliferative p24-specific T-helper cell responses in the LTNP CDT-01. The immunodominant response was to the peptide DRVHPVHAGPIAPGQMREPRGS (81-102), and 9/10 CD4+ T-cell clones reacted with it. One was characterized in detail and used a Bβ4 TCR.
- The minimum peptide recognized by the clones from CDT-01 was VHAGPIAPG and it was restricted by HLA-DQ7.

HXB2 Location p24 (86–94)
Author Location p24 (219–227 NY-5)
Epitope VHAGPIAPG
Epitope name VG9
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DQ7)
Donor MHC DR11, DR15, DRw51, DRw52, DQ6, DQ7
Country United States.
Assay type proliferation, CD4 T-cell Elispot - IFNγ
Keywords acute infection, early treatment, variant cross-recognition or cross-neutralization
References Norris *et al.* 2004

- Five CD4-T cell epitopes in Gag-p24 were studied, and a minimum epitope length of 6-16 amino acids were found to be required for CD4+ T cell proliferation. Cross-clade recognition was studied and found to be impaired in 17/32 variants tested.
- Patient CTS01, who was infected with HIV-1 in 1998, was a long term non-progressor, and recognized this epitope.
- This epitope,VHAGPIAPG was the most variable of the five epitopes studied. Only the C variant Ihagpiapg did not diminish the response. All other variations imparied responses: vhagpVapg, found in clades A, B, C, and D; vQagpVapg,clades B, C, D; AQagpFPpg, IhagpVapg, AhagpVapg, and vQagpiP, all found in clade A; AQagpiapg, clade B; and vPagpiapg, clade C.
- Minimum length peptides for the epitopes studies were not particularly optimal, and peptides longer than the minimum, up to 22 amino acids, were often as potent, in marked contrast to CD8+ T cell responses.

HXB2 Location p24 (87–101)
Author Location p24 (219–233 BRU)
Epitope HAGPIAPGQMREPRG
Immunogen in vitro stimulation or selection
Species (MHC) mouse (H-2^b)
References Vaslin *et al.* 1994

- Peptide G2: could prime for *in vitro* immunoproliferative responses and for subsequent IgG responses.

HXB2 Location p24 (96–103)
Author Location p24 (228–235 LAI)
Epitope MREPRGSD
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location p24 (96–110)
Author Location p24 (228–242 IIIB, B10)
Epitope MREPRGSKIAGTTST
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location p24 (98–107)
Author Location p24 (231–240 NY-5)
Epitope EPRGSDIAGT
Epitope name ET10
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DQ7)
Donor MHC DR11, DR14, Drw52, DQ3, DQ5
Country United States.
Assay type proliferation, CD4 T-cell Elispot - IFNγ, Chromium-release assay
Keywords acute infection, early treatment, variant cross-recognition or cross-neutralization
References Norris *et al.* 2004

- Five CD4-T cell epitopes in Gag-p24 were studied, and a minimum epitope length of 6-16 amino acids were found to be required for CD4+ T cell proliferation. Cross-clade recognition was studied and found to be impaired in 17/32 variants tested.
- Patient AC-01, who was infected with HIV-1 in 1997, recognized this epitope and epitope EPRGSDIAGT during acute infection, and 19 months post-initiation of ART therapy started during primary infection.
- This was the most variable of the five epitopes studied. REPRGSDIAGT natural variants were tested and did not usually diminish the response by much (rDprgsdiagt, clades B and C; and rDprgsdiagA and rGprgsdiagt, both clade C), although the CRF01 AE variant reprgAdiagt abrogated the response.
- Minimum length peptides for the epitopes studies were not particularly optimal, and peptides longer than the minimum, up to 22 amino acids, were often as potent, in marked contrast to CD8+ T cell responses. This peptide was the exception, as REPRGSDIAGTT, which is elongated by 2 amino acids compared to the minimum epitope, elicited a stronger proliferative immune response as well as IFN-gamma secretion and cytolyis.

HXB2 Location p24 (99–118)
Author Location p24 (231–250 IIIB)
Epitope PRGSDIAGTTSTLQEQIGWM
Epitope name P24
Immunogen in vitro stimulation or selection
Species (MHC) human (DR4)
Donor MHC DR4, DR7 DQ2 and DQ3
Keywords immunodominance, Th1, Th2, TCR usage
References Venturini *et al.* 2002

- PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA class II DR restricted.
- Clone 6 recognized three peptides including this one with a Th1 response using TCR Vβ 6 (6s5A1N1). Sequencing TCR Vβ regions of colonies from clone 6 suggested this was a clonal population. Assays using different peptide concentrations suggest that this peptide does not carry the main epitope of this clone.

HXB2 Location p24 (101–115)
Author Location p24 (235–249 SF2)
Epitope GSDIAGTTSTLQEQI
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* B clade SF2 *HIV component:* p24 Gag
Species (MHC) macaque
References Mills *et al.* 1990

- Responses to 3 T-cell and multiple linear B-cell epitopes were found in vaccinated macaques – epitope response defined by T-cell clone.

HXB2 Location p24 (101–116)
Author Location p24
Epitope GSDIAGTTSTLQEQIC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.

HXB2 Location p24 (109–128)
Author Location p24 (241–260 IIIB)
Epitope STLQEQIGWMTNNPPIPVGE
Epitope name P25
Immunogen in vitro stimulation or selection
Species (MHC) human
Donor MHC DR4, DR7 DQ2 and DQ3
Keywords immunodominance, Th1, Th2, TCR usage
References Venturini *et al.* 2002

- PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA class II DR restricted.
- Clone 50 recognized this peptide with a Th0 response (Th0 means that cytokines characteristic of both Th1 and Th2 responses were stimulated), using TCR Vβ 17, and was a homogeneous T-cell population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.

HXB2 Location p24 (111–132)
Author Location p24 (243–264 SF2)
Epitope LQEQIGWMTNNPPIPVGEIYKR
Immunogen HIV-1 infection
Species (MHC) human
References Rosenberg *et al.* 1997

- Low viral load correlated with strong HIV-1-specific proliferative response.
- A proliferative response to this epitope was detected in two long term survivors.

HXB2 Location p24 (119–133)
Author Location p24 (251–265)
Epitope TNNPPIPBGEIYKRW
Immunogen HIV-1 infection
Species (MHC) human (DRB1*1301)
Keywords binding affinity, HAART, ART
References Blankson & Siliciano 2001; Malhotra *et al.* 2001

- The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months.
- PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment.
- DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (LTNPs) (it was in 9/18 versus, versus 21% of the general population)
- This epitope was mapped with truncated peptides using the Elispot assay.
- Two distinct DRB1*13 epitopes were defined in the peptide region spanning 251 to 270, and this 20-mer bound with very high affinity to DRB1*1302 – DRB1*1301 and DRB1*1302 would be expected to have very similar binding properties.

HXB2 Location p24 (121–136)
Author Location p24 (253–267)
Epitope NPPIPVGEIYKRWIIC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.

HXB2 Location p24 (121–140)
Author Location Gag (253–272 SF2)
Epitope NPPIPVGEIYKRWILGLNK
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade SF2 *HIV component:* p24 Gag
Species (MHC) mouse (H-2^d)
Keywords immunodominance, Th1
References Mata & Paterson 1999

- Listeria moncytogenes is an intracellular bacterium that lives in the cytoplasm and generates a cell-mediated immune response.

- Listeria moncytogenes vaccine expressing HIV-1 p24 protein (Lm-Gag) was used to stimulate gag specific CD4+ T cell proliferative responses in BALB/c(H-2d) and C57BL/6(H-2b) mice.
- Two of three reactive p24 peptides (out of 22 overlapping peptides that span p24) were recognized by both murine strains – this epitope is immunodominant in BALB/c mice and did not stimulate a C57BL/6 response.
- The proliferative response is due to CD4+, IFNγ producing cells, a Th1 response.

HXB2 Location p24 (121–140)
Author Location p24 (253–272 HXB2)
Epitope NPPIPVGEIYKRWIILGLNK
Subtype B
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2^d)
Keywords immunodominance
References Mata & Paterson 1999

- BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.
- The class II T helper response was probed using 20 mer peptides that overlapped by 10, and the peptide MPPIPVGEIYKRWIILGLNK gave the immunodominant response for the H-2^d haplotype, but was not recognized in H-2^b mice.

HXB2 Location p24 (121–140)
Author Location Gag (197–205)
Epitope NPPIPVGEIYKRWIILGLNK
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2d)
Country United States.
Assay type proliferation, T-cell Elispot
Keywords vaccine antigen design
References Kwak *et al.* 2004

- A recombinant vaccinia virus with HIV-1 Gag replacing the cytoplasmic domain of the B5R protein was shown to induce better primary CD4 response than recombinant vaccinia virus expressing Gag from the TK-locus; CD8 responses were less specific. When immunized BALB/c mice were challenged with a recombinant Listeria that expresses HIV-Gag, lower colony counts of Listeria were found in the liver and spleen of mice immunized with virus expressing B5R-Gag fusion protein.

HXB2 Location p24 (121–152)
Author Location Gag (183–214 LAI)
Epitope NPPIPVGEIYKRWIILGLNKIVRMYSPTSILD
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 9/10 reacted to this peptide.
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in four vaccinees.
- All of the 12 tested had an IgG response to this peptide.

HXB2 Location p24 (127–141)
Author Location Gag (294–308)
Epitope GEIYKRWIILGLNKI
Epitope name Gag 294
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicted proliferative responses from multiple HIV-infected donors.
- This epitope binds ten HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101 with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 95% of clade B isolates.
- 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location p24 (127–141)
Author Location p24 (294–308)
Epitope GEIYKRWIILGLNKI
Epitope name Gag2
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Country United Kingdom.
Assay type cytokine production, proliferation
Keywords supertype, rate of progression
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.

HXB2 Location p24 (128–137)
Author Location p24 (260–269)
Epitope EIYKRWIILG
Immunogen HIV-1 infection
Species (MHC) human (DRB1*1301, DRB1*1302)
Keywords binding affinity, HAART, ART, Th1
References Blankson & Siliciano 2001; Malhotra *et al.* 2001

- The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months.
- PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment.
- DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (it was in 9/18 versus, versus 21% of the general population)
- The truncated peptide that gave the optimal proliferative response for a Th1 phenotype clone was this nine-mer.
- This region, shared by 2 overlapping peptides, was the reactive region for clones from two DRB1*13 patients, one carried DRB1*1301 and one DRB1*1302.
- Two distinct epitopes were defined in the peptide region spanning 251 to 270, and this 20-mer bound with very high affinity to DRB1*1302 – DRB1*1301 and DRB1*1302 would be expected to have very similar binding properties.

HXB2 Location p24 (129–148)
Author Location p24 (261–280 IIIB)
Epitope IYKRWIILGLNKIVRMYSPT
Epitope name P27
Immunogen in vitro stimulation or selection
Species (MHC) human
Donor MHC DR4, DR7 DQ2 and DQ3
Keywords immunodominance, Th1, Th2, TCR usage
References Venturini *et al.* 2002

- PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA class II DR restricted.
- Clone 74 recognized two peptides including this one with a Th1 response using TCR Vβ 13 (13s1); it required 200 ng/ml (100 nM) and 1 µg/ml (0.5 µM) for stimulation by peptides 480-500 and 261-280, respectively. Sequencing TCR Vβ regions of colonies from clone 74 suggested this was a clonal population.

HXB2 Location p24 (131–145)
Author Location p24 (265–279 SF2)
Epitope KRWIILGLNKIVRMY
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* B clade SF2 *HIV component:* p24 Gag
Species (MHC) macaque
References Mills *et al.* 1990

- Responses to 3 T-cell and multiple linear B-cell epitopes were found in vaccinated macaques – epitope response defined by T-cell clone.

HXB2 Location p24 (131–145)
Author Location Gag (298–312)
Epitope KRWIILGLNKIVRMY
Epitope name Gag 298
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds thirteen HLA-DR alleles: DRB4*0101, DRB5*0101, DRB1*0901, DRB1*0802, DRB1*0701, DRB1*1302, DRB1*1201, DRB1*1101, DRB1*0405, DRB1*0401, DRB*0301, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 94% of clade B isolate.
- 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location p24 (131–145)
Author Location p24 (298–312)
Epitope KRWIILGLNKIVRMY
Epitope name Gag3
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Country United Kingdom.
Assay type proliferation, Intracellular cytokine staining
Keywords supertype, rate of progression
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.

HXB2 Location p24 (131–152)
Author Location p24 (263–284 SF2)
Epitope KRWIILGLNKIVRMYSPTSILD
Immunogen HIV-1 infection
Species (MHC) human
References Rosenberg *et al.* 1997

- Low viral load correlated with strong HIV-1-specific proliferative response.
- A proliferative response to this epitope was detected in two long term survivors.

HXB2 Location p24 (133–144)
Author Location p24 (133–144 B Consensus)
Epitope WIILGLNKIVRM
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DRB1*1101, DRB1*1302, DRB1*1501, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This is the core of the peptide was very often recognized, with a responses by 25% of the study group. The core epitope, WIILGLNKIVRM, could bind 5/8 HLA-DR molecules tested.

HXB2 Location p24 (133–150)
Author Location p24 (133–150 B Consensus)
Epitope WIILGLNKIVRMYSPTSI
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DRB1*0401, DRB1*0405, DRB1*0701, DRB1*1101, DRB1*1302, DRB1*1501, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 25% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.
- The peptides that were recognzied by the most people were able to bind broadly to multiple HLA-DR molecules. This peptide showed very high cross-reactive binding capacity, and bound to 8/8 tested common HLA-DR molecules.

HXB2 Location p24 (135–145)
Author Location p24 (135–145 B Consensus)
Epitope ILGLNKIVRMY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0401, DRB1*1302, DRB1*1501)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This is the core of the peptide was very often recognized, with a responses by 25% of the study group. The core epitope, ILGLNKIVRMY, could bind 3/8 HLA-DR molecules tested.

HXB2 Location p24 (135–154)
Author Location p24 (267–286)
Epitope ILGLNKIVRMYSPTSILDIR
Immunogen HIV-1 infection
Species (MHC) human
References Adams *et al.* 1997

- One of four immunogenic Gag peptides used in study of the proliferative response to p24.
- 8 of 24 HIV+ individuals responded to this epitope.
- Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response.

HXB2 Location p24 (139–148)
Author Location p24 (271–280 HZ321)
Epitope NKIVRMYSPT
Subtype AG
Immunogen Vaccine

Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA), CpG immunostimulatory sequence (ISS)
Species (MHC) macaque
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords vaccine-induced epitopes, adjuvant comparison, vaccine antigen design
References Silvera *et al.* 2004

- Macaques were immunized with gp120-depleted HIV-1 together with incomplete Freund's adjuvant and CpG-ODN. All four immunized animals had high anti-p24 antibody titers, while three animals showed HIV-1-specific CD4+ and CD8+ T-cell responses. This is one of two CD4+ T-cell epitopes in Gag that was mapped.

HXB2 Location p24 (139–157)
Author Location p24 (271–290 IIIB)
Epitope NKIVRMYSPTSILDIRQGP
Epitope name P28
Immunogen in vitro stimulation or selection
Species (MHC) human (DR4)
Donor MHC DR4, DR7 DQ2 and DQ3
Keywords immunodominance, Th1, Th2, TCR usage
References Venturini *et al.* 2002

- PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA class II DR restricted.
- Clone 6 recognized three peptides including this one with a Th1 response using TCR Vβ 6 (6s5A1N1). Sequencing TCR Vβ regions of colonies from clone 6 suggested this was a clonal population. Assays using different peptide concentrations suggest that this peptide, 271-290, contains the main epitope of this clone. Upon activation, clone 6 was observed to induce a cytopathic effect in the adherent layer of fibroblasts expressing HLA DR4W14 and -W15. Clone 6 was activated in response to vaccinia virus Gag-infected B-LCL, so it could recognize naturally processed epitopes.
- Clone 37 recognized this peptide sequence with a Th2 response using TCR Vβ 3, and was a homogeneous T-cell population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.
- Clone 97 recognized this peptide sequence with a using TCR Vβ 9 and 14; the two TCR receptors used indicates this limiting dilution represents a mixed population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.

HXB2 Location p24 (140–148)
Author Location p24 (272–280 HXB2)
Epitope KIVRMYSPT
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRβ1*0101)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords HAART, ART
References Boritz *et al.* 2003

- HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells/ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.
- The Th clone that recognized this epitope utilized TCR Vβ 5.2.

HXB2 Location p24 (141–156)
Author Location p24 (273–287)
Epitope IVRMYSPTSILDIRQC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.
- Matches 3/3 anchor residues for HLA DR: **I**VRMY**S**PT**S**

HXB2 Location p24 (141–158)
Author Location p24 (141–158 B Consensus)
Epitope IVRMYSPTSILDIRQGPK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 17% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term

non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p24 (146–160)
Author Location p24 (278–292 IIIB, B10)
Epitope SPTSILDIRQGPKEP
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location p24 (149–168)
Author Location p24 (281–300 IIIB)
Epitope SILDIRQGPKEPFRDYVDRF
Epitope name P29
Immunogen in vitro stimulation or selection
Species (MHC) human (DR4)
Donor MHC DR4, DR7 DQ2 and DQ3
Keywords immunodominance, Th1, Th2, TCR usage
References Venturini *et al.* 2002

- PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA class II DR restricted.
- Clone 6 recognized three peptides including this one with a Th1 response using TCR Vβ 6 (6s5A1N1). Sequencing TCR Vβ regions of colonies from clone 6 suggested this was a clonal population. Assays using different peptide concentrations suggest that this peptide does not carry the main epitope of this clone.

HXB2 Location p24 (150–169)
Author Location p24 (282–301)
Epitope ILDIRQGPKEPFRDYVDRFY
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location p24 (151–166)
Author Location p24 (283–297)
Epitope LDIRQGPKEPFRDYVC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.

HXB2 Location p24 (155–177)
Author Location p24 (287–309)
Epitope QGPKEPFRDYVDRFYKTLRAEQA
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse
References Nakamura *et al.* 1997

- Mice immunized with this peptide generated proliferative responses, CTLs and antibodies.
- This immunogenic domain is from a highly conserved region of p24.

HXB2 Location p24 (156–170)
Author Location p24 (288–302 IIIB, B10)
Epitope GPKEPFRDYVDRFYK
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location p24 (156–173)
Author Location p24 (156–173 B Consensus)
Epitope GPKEPFRDYVDRFYKTLR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p24 (156–174)
Author Location p24 (287–306)
Epitope QPKEPFRDYVDRFYKTLRA
Immunogen HIV-1 infection
Species (MHC) human
References Adams *et al.* 1997

- One of four immunogenic Gag peptides used in study of the proliferative response to p24.
- T-cells from 5 of 21 HIV+ individuals responded to this epitope.
- Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response.

HXB2 Location p24 (157–165)
Author Location p24 (289–297 HXB2)
Epitope PKEPFRDYV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DQ5)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords HAART, ART
References Boritz *et al.* 2003

- HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.

HXB2 Location p24 (161–180)
Author Location Gag (293–312 SF2)
Epitope FRDYVDRFYKTLRAEQASQD
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade SF2 *HIV component:* p24 Gag
Species (MHC) mouse (H-2^d, H-2^b)
Keywords Th1
References Mata & Paterson 1999

- Listeria moncytogenes is an intracellular bacterium that lives in the cytoplasm and generates a cell-mediated immune response.
- Listeria moncytogenes vaccine expressing HIV-1 p24 protein (Lm-Gag) was used to stimulate gag specific CD4+ T cell proliferative responses in BALB/c(H-2d) and C57BL/6(H-2b) mice.
- Two of three reactive p24 peptides (out of 22 overlapping peptides that span p24) were recognized by both murine strains – this peptide stimulated a response in both BALB/c and C57BL/6 mice.
- The proliferative response is due to CD4+, IFNγ producing cells, a Th1 response.

HXB2 Location p24 (161–180)
Author Location p24 (293–312 HXB2)
Epitope FRDYVDRFYKTLRAEQASQD
Subtype B
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2^d, H-2^b)
References Mata & Paterson 1999

- BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.
- The class II T helper response was probed using 20 mer peptides that overlapped by 10, and the peptides VHQAISPRTLNAWVKVVEEK and FRDYVDRFYKTLRAEQASQD were recognized in H-2^b and H-2^d mice.

HXB2 Location p24 (163–175)
Author Location Gag (295–307)
Epitope DYVDRFYKTLRAE
Immunogen HIV-1 infection
Species (MHC) human (DR0101)
Assay type cytokine production, proliferation, Tetramer binding, CD4 T-cell Elispot - IFNγ
Keywords HAART, ART, supervised treatment interruptions (STI)
References Iyasere *et al.* 2003

- Fifteen patients recieving HAART with strong CD4+ proliferative responses to HIV antigens while on therapy were examined, to see the effects of viremia on these responses during treatment interruptions. Increased viremia occurred in 12/15 patients during at least one treatment interruption. Anti-HIV proliferative responses were inhibited during viremia, but IFNgamma production to Gag, Pol, and Nef peptide pools were maintained.
- IL-2 production diminished during viremia, and exogenous IL-2 revived *in vitro* proliferation of HIV-specific T-cells to Gag or Pol DR0101 epitopes in a tetramer, as well as Gag-specific total CD4 T-cell responses.

HXB2 Location p24 (163–177)
Author Location p24 (295–309)
Epitope DYVDRFYKTLRAEQA
Immunogen HIV-1 infection
Species (MHC) human (DRB1*1302)
Keywords HAART, ART
References Blankson & Siliciano 2001; Malhotra *et al.* 2001

- The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months.
- PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment.
- DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (it was in 9/18 versus, versus 21% of the general population)
- This epitope was mapped with truncated peptides using the Elispot assay, and is highly conserved.

HXB2 Location p24 (163–177)
Author Location p24 (295–309)
Epitope DYVDRFYKTLRAEQA
Immunogen HIV-1 infection
Species (MHC) human (DRB1*1302)
Keywords HAART, ART

References Blankson & Siliciano 2001; Malhotra *et al.* 2001

- The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months.
- PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment.
- DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (it was in 9/18 versus, versus 21% of the general population)
- This epitope was mapped with truncated peptides using the Elispot assay, and is highly conserved.

HXB2 Location p24 (164–181)
Author Location p24 (164–181 B Consensus)
Epitope YVDRFYKTLRAEQASQEV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DRB1*0401, DRB1*0405, DRB1*0701, DRB1*1101, DRB1*1302, DRB1*1501, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The peptides that were recognzied by the most people were able to bind broadly to multiple HLA-DR molecules. This peptide showed very high cross-reactive binding capacity, and bound to 8/8 tested common HLA-DR molecules.
- This peptide was the most often recognized, with a responses by 58% of the study group.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p24 (167–178)
Author Location p24 (167–178 B Consensus)
Epitope RFYKTLRAEQAS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DRB1*0401, DRB1*0405, DRB1*0701, DRB1*1101, DRB1*1501, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This is the core of the peptide was the most often recognized, with a responses by 58% of the study group. The core epitope, RFYKTLRAEQAS, could bind 7/8 HLA-DR molecules tested.

HXB2 Location p24 (168–179)
Author Location p24 (168–179 B Consensus)
Epitope FYKTLRAEQASQ
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DRB1*0401, DRB1*1101, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This is the core of the peptide was the most often recognized, with a responses by 58% of the study group. The core epitope, FYKTLRAEQASQ, could bind 4/8 HLA-DR molecules tested.

HXB2 Location p24 (168–180)
Author Location p24 (168–180 B Consensus)
Epitope FYKTLRAEQASQE
Subtype B
Immunogen HIV-1 infection

Species (MHC) human (DRB1*0101, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*1501, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This is the core of the peptide was the most often recognized, with a responses by 58% of the study group. The core epitope, FYKTLRAEQASQE, could bind 6/8 HLA-DR molecules tested.

HXB2 Location p24 (169–177)
Author Location p24 (169–177 B Consensus)
Epitope YKTLRAEQA
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- This is the core of the peptide was the most often recognized, with a responses by 58% of the study group. This core epitope could bind only 1/8 of HLA-DR molecules tested.

HXB2 Location p24 (169–178)
Author Location p24 (301–310 HZ321)
Epitope YKTLRAEQAS
Subtype AG
Immunogen Vaccine
Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA), CpG immunostimulatory sequence (ISS)
Species (MHC) macaque
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords vaccine-induced epitopes, adjuvant comparison, vaccine antigen design
References Silvera *et al.* 2004

- Macaques were immunized with gp120-depleted HIV-1 together with incomplete Freund's adjuvant and CpG-ODN. All four immunized animals had high anti-p24 antibody titers, while three animals showed HIV-1-specific CD4+ and CD8+ T-cell responses.

HXB2 Location p24 (175–199)
Author Location p17 (307–331 PV22)
Epitope EQASQEVKNWMTETLLVQNANPDCK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*03)
Donor MHC A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13
Keywords HAART, ART, Th1, Th2, TCR usage
References Lotti *et al.* 2002

- 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response.
- For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity.
- 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 26 recognized this peptide sequence restricted by DRB1*03. This clone had a SI of 4.1 to p55, 5.3 to peptide, secreted high levels of IFNγ, indicative of a Th1 response, but also IL-4 and IL-5. Clone 26 had no cytotoxic activity.

HXB2 Location p24 (181–198)
Author Location p24 (313–327)
Epitope VKNWMTETLLVQNANC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Bedford *et al.* 1997

- Epitope elicits a primary proliferative response in PBMC from uninfected donors.
- Matches 3/3 anchor residues for HLA DR: **V**KNWM**T**ET**L**

HXB2 Location p24 (185–202)
Author Location p24 (185–202 B Consensus)
Epitope MTETLLVQNANPDCKTIL
Subtype B

Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p24
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A01, A32, B*1410, B15; A*3101, A68, B*4403, B51
Country Spain.
Assay type proliferation, CD4 T-cell Elispot - IFNγ
Keywords HAART, ART, supervised treatment interruptions (STI)
References Arnedo-Valero *et al.* 2004

- T cell immune responses following STI were monitored in two chronically HIV-1 infected partners (A and B) who had contracted HIV-1 during 1992. STI induced strong transitory CD4+ and CD8+ T cell responses in both patients. The viruses remained very closely related over 10 years, despite the two individuals having different HLA types; the authors suggest the maintained similarity does not support a strong role for HLA driven HIV diversity as has been claimed in Moore et al. (Science 2002).
- During the second treatment stop, patient A developed a strong proliferative response to p24, and multiple strong CD8+ T cell repsonses to Env, Pol, Gag and Nef. This patient was able to control viral load for two years follow up without therapy. Patient B developed a very weak CD4+ T cell response against p24 during breaks in therapy, and had CD8+ responses to two epitopes. Patient A: A01, A32, B*1410, B15; Patient B: A*3101, A68, B*4403, B51.

HXB2 Location p24
Author Location p24
Epitope
Immunogen Vaccine
HIV component: p24 Gag *Adjuvant:* Keyhole Limpit Haemocyanin (KLH)
Species (MHC) human
Country United States.
Assay type proliferation, Th support of CTL response, Delayed-type hypersensitivity (DTH)
Keywords HAART, ART, immune dysfunction
References Lange *et al.* 2004

- ART treated HIV-1 infected patients with strong lymphoproliferative responses to HIV p24 did not have enhanced immune responses relative to those that had low level proliferative responses. Immune function was measured by DTH to diphteria/tetanus-toxoid and Keyhole limpet hemocyanin, maturation and frequency of CD8+ T cells, frequency of CD4 and CD8+ T cells, and cytotoxic molecules on HIV specific T cells.
- A higher level of persistant viral replication in circulating CD4+ cells was associated with patients who showed high lymphoproliferative responses to HIV p24.

HXB2 Location p24
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type proliferation, Intracellular cytokine staining
Keywords HAART, ART, immune dysfunction
References Palmer *et al.* 2004

- The cytokine and maturation profiles as well as the proliferative capacity of HIV-1 Gag-specific CD4+ T cells was analyzed in 4 groups of HIV-1 infected patients: HAART treated, HAART suppressed, treatment naive and untreated, slowly progressing. Measurements of Gag-specific CD4+ T cell maturation, proliferation and plasma viremia indicate that virologic control is impaired due to HIV-1 affects on the maturation profiles of CD4+ T cells.

III-B-3 Gag p2p7p1p6 Helper, CD4+, T-cell epitopes

HXB2 Location p2p7p1p6 (18–37)
Author Location p24 (384–400 HXB2)
Epitope GNFRNQRKIVKCFNCGKEGH
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DR15/51)
Donor MHC DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords HAART, ART
References Boritz *et al.* 2003

- HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells/ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.
- The two Th clones that recognized this epitope utilized TCR Vβ2 and Bβ8.1.

HXB2 Location p2p7p1p6 (30–44)
Author Location p15 (393–407 IIIB, B10)
Epitope FNCGKEGHTARNCRA
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location p2p7p1p6 (37–52)
Author Location p15 (37–52 B Consensus)
Epitope HIAKNCRAPRKKGCWK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 14% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p2p7p1p6 (55–69)
Author Location p15 (418–432 IIIB, B10)
Epitope KEGHQMKDCTERQAN
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location p2p7p1p6 (60–74)
Author Location p15 (423–437 IIIB, B10)
Epitope MKDCTERQANFLGKI
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location p2p7p1p6 (66–81)
Author Location p15 (66–81 B consensus)
Epitope RQANFLGKIWPSHKGR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DR01*0401, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*1501, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 28% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The peptides that were recognzied by the most people were able to bind broadly to multiple HLA-DR molecules.This peptide showed high cross-reactive binding capacity and bound to 7/8 tested HLA-DR molecules.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p2p7p1p6 (72–89)
Author Location p15 (72–89 B Consensus)
Epitope GKIWPSHKGRPGNFLQSR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.

Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 17% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p2p7p1p6 (76–83)
Author Location p24 (439–446 LAI)
Epitope PSYKGRPG
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.
- Schrier lists this peptide as p24(439-446), but because of the numbering used for Gag epitopes, we placed it in p2p7p1p6.

HXB2 Location p2p7p1p6 (83–97)
Author Location p15 (446–460 BRU)
Epitope GNFLQSRPEPTAPPA
Immunogen in vitro stimulation or selection
Species (MHC) mouse (H-2^b)
References Vaslin *et al.* 1994

- Peptide G4: could prime for *in vitro* immunoproliferative responses and for subsequent IgG responses.

HXB2 Location p2p7p1p6 (93–112)
Author Location p15 (93–112 B Consensus)
Epitope TAPPEESFRFGEETTTPSQK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 14% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p2p7p1p6 (98–112)
Author Location p15 (473–487 IIIB, B10)
Epitope ESFRSGVETTTPPQK
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- Peptides were identified that commonly evoke T-cell responses – 50% of 90 HIV+ people had a T-cell response to this peptide.

HXB2 Location p2p7p1p6 (103–110)
Author Location p24 (466–473 LAI)
Epitope REETTTPS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.
- Schrier lists this peptide as p24(466-473), but it is in p2p7p1p6.

HXB2 Location p2p7p1p6 (111–127)
Author Location p15 (111–127 B Consensus)
Epitope QKQEPIDKELYPLASLR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 17% of the study group.

- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location p2p7p1p6 (117–137)
Author Location Gag p6 (480–500 IIIB)
Epitope DKELYPLTSLRSLFGNDPSSQ
Immunogen in vitro stimulation or selection
Species (MHC) human
Donor MHC DR4, DR7 DQ2 and DQ3
Keywords immunodominance, Th1, Th2, TCR usage
References Venturini *et al.* 2002

- PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA class II DR restricted.
- Clone 74 recognized two peptides, including this one, with a Th1 response using TCR Vβ 13 (13s1); it required 200 ng/ml (100 nM) and 1 µg/ml (0.5 µM) for stimulation by peptides 480-500 and 261-280, respectively. Sequencing TCR Vβ regions of colonies from clone 74 suggested this was a clonal population. Clone 74 was activated in response to vaccinia virus Gag-infected B-LCL, so it could recognize naturally processed epitopes.

HXB2 Location p2p7p1p6 (118–137)
Author Location p15 (118–137 B Consensus)
Epitope KELYPLASLRSLFGNDPSSQ
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 17% of the study group.

- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

III-B-4 Gag Helper, CD4+, T-cell epitopes

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection, Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* p17 Gag, p24 Gag
Species (MHC) human
References Kelleher *et al.* 1998b

- Immunization of HIV+ people with a p24-VLP virus-like particle did not significantly impact CD4+ lymphocyte count, viral load, or p24 antibody titre.
- Immunization with p24-VLP showed a modest, short-lived increased proliferative response to p24.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection, Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)), protein *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus, p24 Gag
Species (MHC) human
References Maino *et al.* 2000

- 18 HIV-1-seropositive patients with a low frequency or no detectable CD4+ T cell response to HIV-1 antigen received an HIV-1 immunogen consisting of 10 units of native p24 and 100 ug of HZ321, a gp120 depleted antigen.
- Using flow-cytometric methods, HIV-1 specific CD4+ T cells were shown to increase in response to immunization – in many patients significant enhancement was observed after a single immunization.
- The frequency of CD4+ T cells expressing cytokines in response to antigen by FACS was correlated with a lymphoproliferation assay.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human

Keywords HAART, ART, supervised treatment interruptions (STI)
References Ruiz *et al.* 2000

- Structured treatment interruption in chronically infected patients allowed recovery of p24 Th proliferative responses after HAART therapy discontinuation in 2/12 patients.
- The Th response to p24 was identified during peak viremia in one patient, while in the second it was noted when viremia was controlled after restarting antiviral therapy.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Lori *et al.* 1999

- Ten patients with acute, pre-seroconversion HIV-1 infections were treated with didanosine, indinavir and hydroxyurea – this treatment is associated with normalization of immune parameters.
- A vigorous HIV-specific Th response (stimulation index greater than 8) was observed in 7/8 patients treated before complete WB seroconversion, but in only 1/5 controls treated after seroconversion.
- Vigorous Th responses were detected as early as 34 days after treatment begin.
- Patients treated prior to seroconversion had no loss of naive CD4 T lymphocytes, recovery of up to 35% of the naive CD8 cells in several weeks, and a reduced latent viral reservoir.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, supervised treatment interruptions (STI), Th1
References Haslett *et al.* 2000

- 11/22 adult patients on HAART showed strong CD4+ T-cell IFNγ producing Th1 responses to HIV p24.
- The magnitude of the Th1 response correlated with previous interruptions in HAART, suggesting the interruptions primed or boosted the response.
- In contrast, the magnitude of the CD8+ CTL response did not correlate with interruptions in therapy, although a greater breadth in response was associated with interruptions in HAART.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* p17 Gag, p24 Gag
Species (MHC) human
References Klein *et al.* 1997

- Immunization of HIV+ people with a HIV-1 p17/p24 Ty virus-like particle (p24-VLP) resulted in a marginal, short-lived increased proliferative response to p24 and p17 and a transient elevation in viral load.
- Two of four subjects that received 500 or 1000 ug of p24-VLP had an increase in gag-specific CTL.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen Vaccine
Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus
Species (MHC) human
Keywords inter-clade comparisons
References Moss *et al.* 1998

- Immunization with gp120 depleted HZ321 virus (REMUNE^{TM}) triggered an increase in lymphocyte proliferative response to native p24, a clade B virus and clade E viral antigens – Z321 is clade A in env and clade G in gag. Moss *et al.* [1998]

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Rosenberg *et al.* 1999

- This paper reviews the role of T-cells in viral control and HIV disease outcome.
- Strong anti-p24 lymphoproliferative responses were found in seven persons who were treated with potent anti-viral therapy during acute HIV-1 infection syndrome.
- This suggests that Th cells are part of the normal response to HIV-1 infection, but their numbers are rapidly diminished by either being infected during the peak viremia or by activation-induced cell death – if peak viremia can be controlled, a robust anti-p24 Th response can be maintained.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Rosenberg & Walker 1998

- Strong Th responses have been found in rare individuals who effectively maintain low viral loads.
- If aggressive anti-retroviral therapy is given prior to seroconversion, strong helper responses can be maintained.

HXB2 Location Gag
Author Location p17
Epitope
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (MHC) mouse
References Birk *et al.* 1998a

- Different p17 genes derived from the same quasispecies and expressed and purified in E. coli primed different Th 1 and Th 2 subsets in mice, depending on their H-2 type.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Schiller *et al.* 2000

- Study of parameters that might influence the performance or reproducibility of clinical Th proliferative assays.
- HIV-1 replication *in vitro* is unlikely to influence the assay.
- Gag proteins including p17 and possibly p7 as well as p24 perform better than p24 alone.
- Frozen samples can be used in T-proliferative assays, but with lower radiolabled thymidine incorporation.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Pitcher *et al.* 1999

- In contrast to earlier studies suggesting that HIV-1 specific Th responses were eliminated in the early stages of infection in most HIV+ individuals, this paper shows using flow cytometric detection of antigen-induced cytokines that Th-1 CD4+ memory gag-specific Th cells are detectable in most HIV+ subjects.
- Effective anti-viral therapy reduces the frequency of these cells, presumably due to reduced antigenic stimulus.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Plana *et al.* 1998

- Patients from later stages of infection given HAART do not show restoration of HIV-1 specific Th proliferative responses.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Kelleher *et al.* 1998a

- Env and gag Th epitopes were pooled and used to test Th proliferative responses after IL2 therapy – while IL2 therapy causes an increase in CD4+ lymphocyte count, it does not increase HIV-1 specific proliferative responses.

HXB2 Location Gag
Author Location Gag (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA prime with vaccinia boost *Strain:* B clade LAI *HIV component:* Env, Gag
Species (MHC) macaque
Keywords Th1, Th2
References Kent *et al.* 1998

- Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T-cell immunity than either vaccine alone.
- The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env – The Th response happened despite a fall in Ab titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced.

HXB2 Location Gag
Author Location
Epitope
Immunogen Vaccine
Vector/Type: DNA, protein, virus-like particle (VLP), ISCOM
Species (MHC) macaque
Keywords Th1, Th2
References Heeney *et al.* 1999

- Ten different vaccine strategies were evaluated for their ability to protect from infection in a rhesus macaque model using a non-pathogenic SHIV challenge.
- Protection correlated with the magnitude of NAb responses, beta-chemokines, and a balanced Th response.
- DNA, protein+adjuvant, VLP and ISCOM vaccines were tested.
- HIV-1/ISCOMS gave the highest NAb titers, Th1 and Th2 responses, was the only vaccine formulation tested with a detectable CTL response, and gave enhanced beta-chemokine production.

HXB2 Location Gag
Author Location Gag/Pol (MN)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade MN *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86
Species (MHC) chimpanzee
References Kim *et al.* 1998

- Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.

HXB2 Location Gag
Author Location Gag/Pol (LAI, MN)
Epitope
Immunogen Vaccine
Vector/Type: canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease
Species (MHC) human

References Salmon-Ceron *et al.* 1999

- A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy uninfected volunteers.

HXB2 Location Gag
Author Location p55 (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Zhang *et al.* 2001b

- T-helper cell proliferative responses to HIV p24, p55 and gp120 were tested in 27 patients with HIV infection – vigorous responses directed at Gag were detected in ten patients, but an Env specific response was detected in only one patient.
- Untreated patients showed a negative correlation between plasma viral load and HIV p24-specific T-cell responses, and the responses could be detected after extended HAART therapy with viremia below the detection limit.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, supervised treatment interruptions (STI), kinetics, Th1
References Carcelain *et al.* 2001

- Repeated structured HAART therapy interruptions (STI) in 3 chronically HIV infected patients induced rapid but transient (< 3 weeks) HIV-1 specific CD4+ Th1 responses concurrently with viral rebound, as measured by proliferation assays and by IFNγ production by CD8-depleted PBMC.
- Kinetics suggest that viral replication leads to rapid destruction of the HIV-specific Th1 cell response.
- HIV-specific CD8+ T-cell responses were delayed relative to the Th1 responses and were not sustained.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Blankson *et al.* 2001

- 5/10 chronically HIV infected patients with low CD4+ counts who received HAART therapy and experienced immune reconstitution displayed p24, p17 and p66 T-helper CD4 proliferative responses, in contrast to 0/8 chronically HIV infected patients with high CD4+ counts at the initiation of antiretroviral treatment.
- This surprising result could be due to the low CD4 nadir patients being more likely to have thymic regeneration or a peripheral expansion of T cells.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Angel *et al.* 2001

- Prolonged viral suppression resulting from potent antiretroviral therapy allowed a T helper response to Gag p24 and PHA to develop in many HIV+ patients.
- At baseline, 2/41 (4.9%) subjects had a proliferative response to Gag p24, and 7/41 (17.1%) had a response to PHA, but by week 72 of therapy, 53% had a detectable response to p24 and 94% to PHA.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Blazevic *et al.* 2000

- Prolonged viral suppression resulting from potent antiretroviral therapy did not allow an HIV T helper response to p24 or gp160, but Th proliferative responses to influenza, alloantigen, and PHA did develop in many HIV+ patients, and asymptomatic patients had stronger and more frequent Th response recovery than AIDS patients.

HXB2 Location Gag
Author Location Gag (SF2)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, acute infection
References Altfeld *et al.* 2001b

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the CTL response was determined using Elispot by studying 19 individuals with preseroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Individuals who were given HAART during acute or early in infection had significantly stronger proliferative responses than individuals who were chronically infected.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their

CTL responses when HAART was eventually given and their viral loads became undetectable.
- In 3/4 responders tested p24 gave the strongest T helper response.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen Vaccine
Vector/Type: gp120 depleted whole killed virus *Strain:* AG recombinant HZ321 *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA), CpG immunostimulatory sequence (ISS)
Species (MHC) rat
References Moss *et al.* 2001
- Different HIV strains were used for different regions: subtype A env, subtype G gag
- Lewis rats simultaneously immunized with HIV-1 antigen and with immunostimulatory sequences CpG had increased Th proliferative responses, but when CpG was given as a prime prior to the injection of HIV-1 antigen it was not as effective.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen Vaccine
Vector/Type: gp120 depleted whole killed virus *Strain:* AG recombinant HZ321 *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA), CpG immunostimulatory sequence (ISS)
Species (MHC) rat
References Moss *et al.* 2000
- Different HIV strains were used for different regions: subtype A env, subtype G gag
- Lewis rats co-immunized with HIV-1 antigen in Freund's and with immunostimulatory sequences CpG stimulated increased IFNγ expressing CD4+ and CD8+ T cells and anti-p24 antibodies relative to antigen in Freund's without CpG.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1
References Kalams *et al.* 1999a
- The strength of p24 specific Gag proliferative responses (SIs) were inversely correlated with viral load in 21 ARV naive patients. The responses were Th1, IFNγ producing. Proliferative responses against gp160 were rarely observed (only 4 cases).
- Gag specific CTL levels were correlated with Gag proliferative responses but were not correlated with viral load. 8 subjects lacked p24 specific Gag proliferative responses, and 4/8 had no CTLp to any HIV-1 antigen tested.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, review, rate of progression
References Kalams & Walker 1998
- This paper reviews the role of specific T cell help in many viral infections, and covers the interplay between Th, CTL and survival, and discusses briefly advantages of HAART during acute HIV infection to prevent the early decimation of the Th response in HIV infections.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1, Th2
References Wilson *et al.* 2000b
- Dysfunction of HIV-1 specific proliferative responses, but not responses to other antigens, is evident in HIV-1 progressive disease.
- Vigorous HIV-1 specific responses to p24, Nef and gp120 with SI between 8-99 were seen in 6/7 long term non-progressors (LTNP), the seventh had a borderline responses. IL-2 production was seen in all cases, and IL-4 production was also evident many responses.
- None of the progressors (0/5) had HIV-1 specific proliferative responses, or IL-2 or IL-4 induction.
- Non-HIV antigens (cytomegalovirus, PPD, Staphylococcus enterotoxin B, tetanus toxoid) gave similar responses in HIV-1 + LTNP, progressors, and HIV-1 controls.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1
References Alatrakchi *et al.* 2002
- LTNP co-infected with HCV and HIV showed higher frequencies of Th1 response to both HIV-1 p24 and HCV antigens.
- HIV-1 CD4 Th1 responses in untreated LTNP were inversely correlated with viral load.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Lange *et al.* 2002
- Cross-sectional study compares CD4 T-cell count and age matched untreated HIV-1 + patients (N = 14) with patients undergoing HAART therapy (N = 14).
- The fractions of naive and memory T-cells were comparable for both groups, as were proliferative responses to non-HIV antigens. Lymphocyte proliferation responses to HIV-1 p24 were of greater magnitude in the group treated with HAART (5/10 had SI >10, versus 1/12 in the untreated group), suggesting that ongoing viral replication impairs the anti-Gag response, and the response can be improved and restored through HAART.

- DTH responses to recall antigens were tested, and responses to C. albicans and Trichophyton were comparable in both treated and untreated patients, although patients on therapy had higher responses to mumps.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, inter-clade comparisons, escape, acute infection
References Fidler *et al.* 2002

- 37/45 patients with primary HIV infection underwent a short course of antiretroviral therapy (SCART). 29/37 patients received triple ART therapy and eight patients received four ART drugs. Initiation of SCART was effective in controlling HIV replication by ten weeks in all patients and preserving CD4+ T cell responses for up to 64 weeks after therapy.
- No induction of drug escape mutations was observed, although two individuals had escape mutations in their infecting virus at baseline.
- 34 UK infected patients were clade B infected. 11/45 subjects had non-UK acquired HIV infection, 2 were clade A, 1 was A/E, 1 was C, 1 was "untypable", the rest were B.
- Recombinant HIV-1 derived gp120, p24, p66 and overlapping peptide pools spanning Tat and Nef were employed to measure CD4 T-cell frequencies in ELISPOT assays. The strongest preservation of T helper responses 12 weeks off SCART was seen for p24-specific CD4+ T-cell responses.
- 6/8 of the untreated individuals were tested for CD4+ T-cell responses. 1 had no detectable response. 1 had detectable responses to all HIV-1 proteins tested at baseline, but this narrowed to p24 and gp120, then became undetectable by 52 weeks. 3 had detectable and persistent responses, but only to p24.
- Post-therapy, the average spot forming cells for all proteins tested in 17/37 with 24 weeks of follow up had not declined, although the plasma viral RNA was increasing. SFU using p24 were measurable following SCART and preserved at levels comparable to baseline.

HXB2 Location Gag
Author Location
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* B clade IIIB *HIV component:* p17 Gag, p24 Gag *Adjuvant:* aluminum hydroxide
Species (MHC) human
Keywords rate of progression
References Klein *et al.* 1997; Lindenburg *et al.* 2002

- HIV-1 p17/p24:Ty virus-like particles therapeutic vaccination of 56 HIV-1 infected patients had no effect on disease progression, AIDS and CD4+ T-cell decline in a longitudinal study, despite some evidence suggesting it can enhance Th anti-Gag proliferative responses in HIV+ individuals Klein *et al.* [1997]

HXB2 Location Gag
Author Location p24 (NY5)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection, cross-presentation by different HLA, early treatment
References Norris *et al.* 2001

- Gag-specific CD4+ helper T-cell clones were derived from one long-term non-progressor (LTNP) (CTS-01), and three individuals given therapy during acute infection, two before (AC-01 and AC-36) and one after (AC-25) STI.
- The immunodominant response in LTNP CTS-01 was to peptide 9, and 9/10 clones derived from this patient reacted with it. Three, two, and one clones were obtained from the three patients given therapy. These six clones all reacted with different p24 peptides, and all had peptide induced proliferative responses, IFNgamma production, and cytotoxic responses. The implications of cytoxic responses in CD4+ T-helper cells are discussed.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Palmer *et al.* 2002

- CD4+ T cell proliferative responses from 33 HIV-1 infected patients with HAART suppression were compared to 19 patients with active viral replication (HAART failures and HAART naive). Patients with HAART suppression showed stronger p24- and p66-specific proliferative responses compared to patient groups with active HIV-1 replication, suggesting active viral replication *in vivo* specifically reduces proliferation responses.
- No differences in the frequency of HIV-specific CD4+ T-cells that were positive for cytokine secretion in a flow cytometry assay were found in the HAART suppressed group versus the group with active viral replication.

HXB2 Location Gag
Author Location p24 (SF2)
Epitope
Subtype B, G
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1, Th2
References Imami *et al.* 2002b

- 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile.

- SF2 p24 20mer peptides overlapping by 10 were used to assess the response in the different groups. At least 1/10 and up to 7/10 nonprogressors had a proliferative response with every one of the 22 p24 overlapping peptides. All peptides produced an IL-2 (Th1) response in at least one of the 10 nonprogressors. IL-4 (Th2) responses were strong, but somewhat less comprehensive as 6/22 peptides elicited no IL-4 production, and fewer IL-4 responses were see per peptide. In contrast, only 1/10 progressors had a clear proliferative and IL-2 response to 2/22 peptides, and neither one made an IL-4 response.
- The results taken together suggest that a balanced Th1/Th2 response to HIV is important for viral control in long-term non-progression.
- One immunologically discordant progressor became symptomatic while on the study. He showed a rapid decline in proliferative activity at that point, and a shift from a Th1 to a Th2 IL-4 producing response.

HXB2 Location Gag
Author Location (BRU)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade BRU *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse
References Haas *et al.* 1991

- Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus.
- B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.

HXB2 Location Gag
Author Location Gag (III-B)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* Gag
Species (MHC) mouse
Donor MHC H-2^d
Keywords vaccine-specific epitope characteristics, Th1
References Bojak *et al.* 2002a

- Codon-optimized gag gene DNA vaccines were compared to wild type by vaccination of BALB/c mice. Codon optimized DNA gave a Th1 polarized Th response, a strong antibody response that persisted from more than 20 weeks, and CTL responses, while wild-type DNA induced weak and inconsistent immune respones.

HXB2 Location Gag
Author Location Gag (MN)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords HAART, ART, acute infection
References Malhotra *et al.* 2003

- 92 acute- or early-HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)), protein *Strain:* AG recombinant HZ321 *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human
Assay type cytokine production, proliferation, T-cell Elispot
Keywords HAART, ART, supervised treatment interruptions (STI), immunotherapy
References Moss *et al.* 2003

- Structured treatment interruptions (STIs) were compared in individuals that had been given prior therapeutic vaccines, and those that had not. Therapeutic immunization increased gag p24 stimulated proliferative responses and MIP-1β responses prior to STIs, although total CD4 counts viral RNA levels were unchanged. Proliferative responses and chemokine induction in the vaccinated group correlated with the control of viremia during subsequent STIs.

HXB2 Location Gag
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type proliferation, T-cell Elispot, Intracellular cytokine staining
Keywords supertype
References Papasavvas *et al.* 2003

- Children with full or partial viral supression along with stable CD4+ T cell counts had significantly increased levels of anti-HIV CD4+ T cell proliferative responses, and decreased CD38+ T-cells.
- Preservation of high levels of CD4+ T-cells was associated with a high percentage of CD4+ naive T-cells relative to memory T-cells.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection, Vaccine

Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human
Assay type proliferation, T-cell Elispot, Delayed-type hypersensitivity (DTH)
Keywords HAART, ART, immunotherapy
References Robbins *et al.* 2003

- Augmented Th cell responses to Gag p24 were seen in five out of five chronically infected individuals who had virological control with HAART, after therapeutic immunization with REMUNE (gp120 depleted inactived virus). The magnitude of responses ranged from a 5- to 200-fold increase, with fluctuation in magnitude over time.
- There was no change in the magnitude and breadth of CTL responses, CD4 counts or percentages, or DTH responses.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Donor MHC A1, A2, B8, B44, DR4, DR15; LTNP S24: A2, A11, B55, B57, DR4, DR13; LTNP C135: A1, A33, B50, B57, DR7, DR13
Assay type cytokine production, proliferation, CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords rate of progression, immunodominance
References Wang *et al.* 2002a

- A 51 year old male, infected presumably in 1988, diagnosed seropositive in 1993, has remained asymptomatic and is a long term non-progressor. He had very low proviral copy number in his PBMCs with high levels of G-A hypermutation, resulting in multiple stop codons, and viral replication was not evident. He was heterozygous for the CCR5 delta 32 allele, and has undergone a variety of treatments through the years. T cell responses in this patient and in two additional LTNPs were described, and this patient had particularly intense CD4+ Th responses.
- PBMC from this patient resisted infection from CCR5, CXCR4 and dual-tropic HIV-1 strains. Purified CD4+ T cells became infected, however, without detectable cytopathic effect. CD8+ T cells were shown to protect PBMCs from infection, and this protection was not mediated by IFNgamma. Undefined CD8 T-cell secreted factors were stimulated by Gag, Pol and Nef genes introduced into target cells with vaccinia and processed through a class I pathway were responsible for the protective effect. This factor resembled CAF, the CD8+ cell antiviral factor described in Mackewicz and Levy (ARHR 8:1039, 1992)
- The CD4+ and CD8+ T-cell populations were both strongly skewed toward the CD45RO+ phenotype, many of which were terminally differentiated, CD28-, and expressed the activation markers CD38+ and HLA-DR+. Cell turnover, however, wasn't much elevated as measured by apoptosis or Ki-67+ and Bcl-2 dim expression.
- Vigorous p24-specific Th proliferative responses were observed, and 50% of CD4+ T-cells proliferated in response to p24 Gag, an extraordinary percentage. Responses were also detected against other regions in Gag, gp120 and Nef. It remains unclear how such vigorous Th responses are maintained with undetectable ongoing viral replication.
- Strong CD4+ T-cell IFNgamma Elispot responses were mapped to many peptides in Gag for this patient. T-cells from two other LTNPs were tested here, and they did not react with as many Gag peptides as the main study subject of the paper. NIH reference Gag peptide set was used, but the sequences of the reactive peptides and the precise strain was not indicated in the paper, so we could not record them in the database.
- CD8+ T cell Elispot responses to Gag, Env, Nef, and Pol were detected as well, although CTL were not prominent, consistent with undetectable viremia.
- This subject had strong NAb responses when tested using the X4 primary isolate 228 200.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC)
Assay type proliferation
Keywords HAART, ART
References Sullivan *et al.* 2003

- Lymphoproliferative responses to HIV antigens p24, gp120 and Nef were enhanced in eight patients who were switched from protease inhibitors to non-nucleoside reverse transcriptase inhibitors.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type cytokine production, proliferation
Keywords HAART, ART
References Hardy *et al.* 2003

- Upon initiating HAART, CD4+ T cell proliferative responses in 36 patients were restored to specific antigens, mitogens, and IL-2. Restored recall responses were largely to persistent antigens, and not to HIV-1 or new antigens, and recall responses were associated with IL-2, not IL-4 production.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen HIV-1 and HCV co-infection
Species (MHC) human
Assay type CD4 T-cell Elispot - IFNγ
Keywords HAART, ART, Th1
References Alatrakchi *et al.* 2004

- Treatment with IFNalpha and ribavirin induced a threefold decrease of type 1 T-helper cell frequencies specific for HIV (p24) and CMV in HIV/HCV co-infected patients undergoing HAART therapy, suggesting this therapy might negatively impact viral-specific immune responses.

HXB2 Location Gag
Author Location p24

Epitope
Immunogen HIV-1 infection
Species (MHC) human
Country Spain.
Assay type proliferation
Keywords HAART, ART, supervised treatment interruptions (STI)
References Plana *et al.* 2004

- Study evaluated the dynamics of CD4+ and CD8+ T-cell responses during 4 cycles of STI in 45 patients, who had early-stage, chronic HIV-1 infection. Lymphoproliferative responses (LPRs) increased between the beginning of the first STI cycle through the 4th STI, but then decreased. Viral load at the end of the 4th STI was inversely correlated with p24 LPRs, but the LPRs were transient and after 12 weeks no longer were correlated with low viral low.
- STIs can boost CTL and LPR responses, but the lack of durable T-helper responses leads to lack of long term viral control.

HXB2 Location Gag
Author Location
Epitope
Subtype CRF02_AG
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human
Country Senegal.
Assay type CD4 T-cell Elispot - IFNγ
Keywords rate of progression, variant cross-recognition or cross-neutralization
References Zheng *et al.* 2004

- Gag, Env, Tat, and Nef-specific T-cell responses were evaluated in 68 HIV-1 and 55 HIV-2 infected drug naive, generally asymptomatic, infected Senegalese patients.
- HIV-1 peptides were derived from HIV-1 CRF-02 (HIV-1 A/G, AJ251056)and HIV-2 peptides spanning HIV-2 ROD (M15390).
- Gag specific responses dominated in both groups, but overall magnitude and frequencies did not correlate with viral load or CD4 counts. CD4+ Helper T-cell responses were found in only 8% of HIV-1 + people, but in 48% of HIV-2 + people, suggesting helper T cell responses may contribute to improved control of viremia in HIV-2 infected patients. Lower viral load was associated magnitude of T-cell responses in HIV-1 infection only when the T-cell responses were measured for cross-reactivity with HIV-2.

HXB2 Location Gag
Author Location p24
Epitope
Subtype A, AG, B
Immunogen HIV-1 infection
Species (MHC) human
Country Cote D'Ivoire.
Assay type cytokine production, CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ
Keywords HIV exposed persistently seronegative (HEPS)
References Jennes *et al.* 2004

- Env(gp120)- and Gag(p24)-specific T helper responses were compared between HIV-exposed seronegative (ESN) and seropositive female sex workers in Africa (Abidjan, Cote d'Ivoire).
- HIV-specific CD4+ T cells were detected in both study groups; low level EliSpot responses were found in 8/40 ESN sex workers. The presence of HIV specific CD4+ T-cells was detected by flow cytometry in 3/8 (38%) in the ESN group, was associated with the frequency and not with the duration of HIV exposure. The ESN reponses were detected in women with more clients on the previous working day and more exposures per month.
- B subtype peptides were used to probe these responses because of availability, however the predominant clades circulating in the area are A and CRF02.

HXB2 Location Gag
Author Location p24 (IIIB)
Epitope
Immunogen in vitro stimulation or selection
Species (MHC) human (A*0201)
Keywords dendritic cells
References Engelmayer *et al.* 2001

- Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis *in vitro* by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors.
- Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific IFNγ CD4+ helper T cell responses to Gag from bulk or purified CD4+ T cells.

HXB2 Location Gag
Author Location p55
Epitope
Immunogen HIV-1 infection
Species (MHC) human (DRB1*13, DRB1*03)
Donor MHC A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13
Keywords HAART, ART, Th1, Th2, TCR usage
References Lotti *et al.* 2002

- 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response.
- For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage. Two clones were DRB1*13 restricted and used TCR Vβ 17+19 or 5.1. Three clones were DRB1*03 restricted and used TCR Vβ 22. Some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production).

HXB2 Location Gag
Author Location p24
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Gag

Species (MHC) mouse (H-2^d)
References Qiu *et al.* 2000

- Mice were injected with plasmid DNA at 0, 2 and 4 weeks and lymphocyte proliferation was measured after 6 weeks with recombinant p24 protein.
- Secreted HIV-1 Gag expression vectors generated a stronger response than standard Gag or cytoplasmic Gag expression vectors.
- IFNγ levels were increased compared to an undetectable IL-4 response.
- CTL levels were also increased in secreted Gag expression vaccination studies.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen Vaccine
Vector/Type: DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18
Species (MHC) mouse (H-2^d)
Keywords Th1, Th2
References Billaut-Mulot *et al.* 2001

- DNA vaccinated BALB/c mice primed and boosted with a multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization.
- Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime + DNA boost was more effective than DNA prime + protein boost.
- Immunization with either the multiepitopic DNA or with the mixed DNA vaccine resulted in Th1 cytokines production (IL-2 and IFNγ) in spleen cell cultures stimulated by Tat and Gag, while Th2 cytokines IL-4 and IL-10 production was not detectable.
- Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.

HXB2 Location Gag
Author Location p24
Epitope
Immunogen Vaccine
Vector/Type: coxsackievirus *HIV component:* p24 Gag
Species (MHC) mouse (H-2^d)
References Halim *et al.* 2000

- An avirulent rec coxsackievirus (CB4-P) construct was generated that can express p24 Gag sequences – CB4-P is attenuated even in immunodeficient mice and T help responses can be elicited from peptides embedded in a surface loop of the VP1 capsid.
- This paper describes the vaccine strategy and generation of constructs, and employs amino-terminal fusion of Gag sequences to the viral polyprotein with subsequent cleavage to elicit CTL responses via MHC class I presentation in BALB/c mice.

HXB2 Location Gag
Author Location gp120 (V3) and p24 (IIIB, MN, BH10)
Epitope
Subtype A, B
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* A clade UG5.94UG018, B clade IIIB *HIV component:* Gag, gp120
Species (MHC) mouse (H-2^d)
Keywords inter-clade comparisons
References Buonaguro *et al.* 2002

- Different HIV strains were used for different regions: gp120 A clade UG5.94UG018; Gag HIV-1 IIIB
- BALB/c mice were given intraperitoneal immunization in the absence of adjuvants with virus-like particles (VLPs) expressing recombinant subtype A gp120 and Pr55gag.
- High dose-independent humoral responses were elicited against both gp120 and p24 peptides, and CTL responses were observed against target cells carrying vaccinia expressed gp120 and Gag.

HXB2 Location Gag
Author Location Gag (HXB2)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag
Species (MHC) mouse (H-2^d, H-2^b)
Keywords Th1
References Mata *et al.* 2001

- BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.
- CD4+ Th1 T-cells mediated the Gag specific immunological protection in mice immunized with Lm-Gag and challenged with vaccinia-Gag.
- Gag-specific CTL may enhance viral clearance via IFNγ secretion, but are not essential for immunity.

HXB2 Location Gag
Author Location Gag
Epitope
Immunogen Vaccine
Vector/Type: Listeria monocytogenes *HIV component:* Gag
Species (MHC) mouse (H-2^d, H-2^b)
Keywords review, Th1
References Mata & Paterson 2000

- BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag.
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.

- This article is a review of L. monocytogenes biology and its potential as a vaccine vector for HIV, comparing to other vector systems, and discussing CD4+ Th1 T-cells mediated Gag specific immunological protection in mice and the Gag CTL response.

III-B-5 RT Helper, CD4+, T-cell epitopes

HXB2 Location RT (36–52)
Author Location RT (36–52 BRU)
Epitope EICTEMEKEGKISKIGP
Immunogen HIV-1 infection
Species (MHC) human
References De Groot *et al.* 1991
- 9 out of 17 humans can make strong IL2 responses to this epitope.

HXB2 Location RT (38–52)
Author Location RT (38–52 BRU)
Epitope CTEMEKEGKISKIGP
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: RT
Species (MHC) mouse (H-2^k)
References De Groot *et al.* 1991
- T-cells from RT immunized mice have enhanced proliferative response with peptide.

HXB2 Location RT (39–53)
Author Location RT (194–208)
Epitope TEMEKEGKISKIGPE
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995a
- Protein priming induced T-cells that recognize peptide, 4 clones from a single donor recognized this peptide.

HXB2 Location RT (48–62)
Author Location RT (48–62 BRU)
Epitope SKIGPENPYNTPVFA
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: RT
Species (MHC) mouse (H-2^k)
References De Groot *et al.* 1991
- T-cells from RT immunized mice have enhanced proliferative response with peptide.

HXB2 Location RT (62–77)
Author Location RT (62–77 BRU)
Epitope AIKKKDSTKWRKLVDF
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: RT
Species (MHC) mouse (H-2^k)
References De Groot *et al.* 1991
- T-cells from RT immunized mice have enhanced proliferative response with peptide.

HXB2 Location RT (88–102)
Author Location RT (88–102 BRU)
Epitope WEVQLGIPHPAGLKK
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: RT
Species (MHC) mouse (H-2^{t4})
References De Groot *et al.* 1991
- T-cells from RT immunized mice have enhanced proliferative response with peptide.

HXB2 Location RT (124–138)
Author Location Pol (303–317)
Epitope FRKYTAFTIPSINNE
Epitope name Pol 303
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001
- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds seven HLA-DR alleles: DRB1*0901, DRB1*0802, DRB1*0701, DRB1*0405, DRB1*0401, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 68% of clade B isolates.
- 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location RT (124–138)
Author Location RT (303–317)
Epitope FRKYTAFTIPSINNE
Epitope name Pol1
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Country United Kingdom.
Assay type proliferation, Intracellular cytokine staining
Keywords supertype, rate of progression
References Boaz *et al.* 2003
- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.

HXB2 Location RT (124–138)
Author Location Pol (303–317)

Epitope FRKYTAFTIPSINNE
Epitope name Pol 303
Immunogen Vaccine
Vector/Type: DNA with CMV promotor, peptide *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (I-Ab and HLA-DR)
Donor MHC H-2b
Keywords vaccine-specific epitope characteristics, immunodominance
References Livingston *et al.* 2002

- Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice.
- Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.

HXB2 Location RT (133–147)
Author Location RT (133–147 BRU)
Epitope PSINNETPGIRYQYN
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: RT
Species (MHC) mouse (H-$2^{k, i5}$)
References De Groot *et al.* 1991

- T-cells from RT immunized mice have enhanced proliferative response with peptide.

HXB2 Location RT (144–158)
Author Location RT (144–158 BRU)
Epitope YQYNVLPQGWKGSPA
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: RT
Species (MHC) mouse (H-2^{t4})
References De Groot *et al.* 1991

- T-cells from RT immunized mice have enhanced proliferative response with peptide.

HXB2 Location RT (156–170)
Author Location Pol (335–349)
Epitope SPAIFQSSMTKILEP
Epitope name Pol 596
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds nine HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0901, DRB5*0101 and DRB3*0101, with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 79% of clade B isolates.
- 7/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location RT (156–170)
Author Location RT (335–349)
Epitope SPAIFQSSMTKILEP
Epitope name Pol2
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Country United Kingdom.
Assay type proliferation, Intracellular cytokine staining
Keywords supertype, rate of progression
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.
- Pol2 was 1 of 3 peptides that had a negative correlation between absolute number of responding cells and viral load.

HXB2 Location RT (156–170)
Author Location Pol (335–449)
Epitope SPAIFQSSMTKILEP
Epitope name Pol 335
Immunogen Vaccine
Vector/Type: DNA with CMV promotor, peptide *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (I-Ab and HLA-DR)
Donor MHC H-2b
Keywords vaccine-specific epitope characteristics, immunodominance
References Livingston *et al.* 2002

- Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice.
- Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG

spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.

HXB2 Location RT (171–189)
Author Location Pol (171–189 HXB2)
Epitope FRKQNPDIVIYQYMDDLYV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DR0101)
Assay type cytokine production, proliferation, Tetramer binding, CD4 T-cell Elispot - IFNγ
Keywords HAART, ART, supervised treatment interruptions (STI)
References Iyasere *et al.* 2003

- Fifteen patients recieving HAART with strong CD4+ proliferative responses to HIV antigens while on therapy were examined, to see the effects of viremia on these responses during treatment interruptions. Increased viremia occurred in 12/15 patients during at least one treatment interruption. Anti-HIV proliferative responses were inhibited during viremia, but IFNgamma production to Gag, Pol, and Nef peptide pools were maintained.
- IL-2 production diminished during viremia, and exogenous IL-2 revived *in vitro* proliferation of HIV-specific T-cells to Gag or Pol DR0101 epitopes in a tetramer, as well as Gag-specific total CD4 T-cell responses.

HXB2 Location RT (171–190)
Author Location RT (171–190 HXB2)
Epitope FRKQNPDIVIYQYMDDLYVG
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DR1, 2 or 3, 4 and 7)
Keywords Th1
References van der Burg *et al.* 1999

- T-cells specific for this epitope from the three donors were stimulated when presented with target cells pulsed with whole RT, indicating that the peptide is naturally processed for multiple HLA-DR molecules.
- Epitope binds to HLA-DR1, -DR2, -DR3, -DR4, and DR7, and can elicit Th1 cells that recognize peptide, protein, and HIV pulsed stimulator cells in the context of DR1, 2 or 3, 4 and 7 – these HLA types cover more than half of the general population.

HXB2 Location RT (171–190)
Author Location RT (171–190 HXB2)
Epitope FRKQNPDIVIYQYMDDLYVG
Subtype B
Immunogen HIV-1 infection, in vitro stimulation or selection
Species (MHC) human (DR1, DR2, DR3, DR4, DR7)
Keywords binding affinity, cross-presentation by different HLA, Th1
References van der Burg *et al.* 1999

- The goal of this study was to identify Th epitopes that could be cross-presented by multiple class II HLA molecules. 5 RT peptides were identified that could bind to more than one HLA class II protein, and but only 2/5 could stimulate strong proliferation responses in PBMC derived from multiple healthy donors.
- This highly conserved epitope binds with high affinity to HLA-DR1, -DR2, -DR3, -DR4, and -DR7 but not HLA-DR5, and stimulated proliferation in 3/3 PBMC individuals with the appropriate HLA alleles.
- This epitope was able to be naturally processed in protein pulsed stimulator cells, and responding clones had a Th1 cytokine profile.
- This epitope is highly conserved and spans the highly conserved YMDD motif, and showing only minor variability in clades A, B, and D.

HXB2 Location RT (195–209)
Author Location RT (IIIB)
Epitope IGQHRTKIEELRQHL
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Protein priming induced T-cells that recognize peptide.

HXB2 Location RT (196–215)
Author Location RT (351–370)
Epitope GQHRTKIEELRQHLLRWGLT
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995a

- Protein priming induced T-cells that recognize peptide, 4 clones from a single donor recognized this peptide.

HXB2 Location RT (249–263)
Author Location RT (IIIB)
Epitope KDSWTWNDIQKLVGK
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming did not induce T-cells that recognize whole protein.

HXB2 Location RT (249–263)
Author Location RT (248–262)
Epitope KDSWTVNDIQKLVGK
Immunogen in vitro stimulation or selection
Species (MHC) human
References De Berardinis *et al.* 1999

- PBMC from donors GD (HLA DR 11; DRB52) and LD (HLA DR 11, 13; DRB52) recognized this epitope (pep23)
- A subset of T-cell lines generated from these donors were capable of recognizing pep23 expressed on the surface of filamentous phage fd, fused to the major coat protein gVIIIp.
- This peptide was selected to study phage presentation of peptide sequences because it was known to serve as a T-cell helper determinant which could induce proliferation from a naive repertoire Manca *et al.* [1995a]

HXB2 Location RT (249–263)
Author Location RT (249–263)
Epitope KDSWTVNDIQKLVGK
Epitope name RT2
Immunogen Vaccine, in vitro stimulation or selection

Vector/Type: HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT
Species (MHC) human (DR5)
Keywords epitope processing
References De Berardinis *et al.* 2000

- Phage display of the CTL epitope, ILKEPVHGV coupled with T helper epitope KDSWTVNDIQKLVGK, elicited specific CTL responses in PBMC from HIV negative individuals and *in vivo* in immunization of HLA-A2 transgenic mice.
- Bacteriophage presentation of peptides is generally used for stimulation of antibodies, and this novel discovery of CTL epitope processing and presentation suggests new possibilities for these vectors.
- HIV-1 peptides were displayed in filamentous bacteriophage fd virion major coat protein pVIII.

HXB2 Location RT (249–263)
Author Location RT (249–263)
Epitope KDSWTVNDIQKLVGK
Epitope name pep23
Immunogen Vaccine, in vitro stimulation or selection
Vector/Type: peptide presented on icosahedral protein scaffold *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human, transgenic mouse (DR5)
Assay type cytokine production, T-cell Elispot, Th support of CTL response
References Domingo *et al.* 2003

- A virus-like protein scaffold, called E2DISP, derived from pyruvate dehydrogenase multienzyme from Bacillus stearothermophilus has been engineered to display 60 copies of one or more epitopes on a single molecule. An E2DISP scaffold which displayed pep23, a 15-residue B and T helper epitope from the reverse transcriptase of HIV-1 elicited a T-helper response *in vitro*.
- The E2DISP scaffold displaying pep23 to stimulate a Th responses, and peptide RT2, which is a CTL epitope from HIV-1 reverse transcriptase, was able to elicit a CD8+ T cell response *in vitro* and in a vaccinated HLA-A2 transgenic mouse. Thus the E2DISP scaffold allows cell-entry and access to the class I and class II processing pathways.
- The Th response in vaccinated mice was also able to support Pep23 specific IgG response.

HXB2 Location RT (249–263)
Author Location RT (248–262)
Epitope KDSWTVNDIQKLVGK
Immunogen in vitro stimulation or selection
Species (MHC) human (DR5-11.01)
Donor MHC DR5, DR6
Assay type proliferation
Keywords binding affinity, epitope processing, vaccine-specific epitope characteristics, escape
References Moschella *et al.* 2003

- Two helper T-cell clones specific for this epitope presented in the context of HLA-DR5-11.01 have been characterized. They have different T cell receptor usage. Residue 11 (kdswtvndiqKlvgk)is a natural variant, and K11A, K11G, K11I, and K11L variants were synthesized and studied in two presentation contexts, one as simple peptides, the other embedded in a recombinant protein, GST.
- The two Th clones and the two presentation contexts gave different outcomes with the peptides. K11I was not stimulatory, and was an antagonist in GST, an agonist as a peptide. K11L retained reactivity when presented in the fusion antigen, and had no acitivity as a peptide. K11G stimualted in both contexts, but the concentrations required for half maximal reactivity were different. K11A could not bind to the MHC in the processed form and could only stimulate when given as a peptide.
- In conclusion, substitutions in epitopes have different effects on Th stimulation depending on the mode of processing, and this should be considered when interpreting Th escape studies and vaccine development.

HXB2 Location RT (249–263)
Author Location RT (248–262)
Epitope KDSWTVNDIQKLVGK
Immunogen in vitro stimulation or selection
Species (MHC) human (DR5-11.01)
Donor MHC DR5, DR6
Assay type proliferation
Keywords binding affinity, epitope processing, vaccine-specific epitope characteristics, escape, TCR usage
References Bonomi *et al.* 2000

- Two helper T-cell clones specific for this epitope presented in the context of HLA-DR5-11.01 have been characterized. One of them used TCR Vβ15, the other used Vβ2. The substituions D2A, W4A, D8A, I9A, and K15A were generated and only D8A, I9A failed to react with one clone, while W4A, D8A, I9A were all critical for a reaction with the other clone, showing the TCRs focused on different but overlapping residues.
- Moving the epitope to different contexts in recombinant proteins for presentation by APCs, as well as adding polyanalanine and polyserine strings to either side of the epitope, influenced reactivity, suggesting processing context can influence the structure of the presentation complex.

HXB2 Location RT (249–263)
Author Location RT (248–262 HXB2)
Epitope KDSSTVNDIQKLVGK
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DRS)
References Fenoglio *et al.* 1999

- RT pep23 epitope exhibited antagonistic activity against proliferation of gp120-specific T-cells when flanked by unrelated amino acid sequence.
- The glutathione S-transferase (GST)-peptide system can be used to display peptides; antigenicity was maintained when this peptide was expressed at the C-term end, but antagonism resulted when this peptide was expressed at the N-term end.

HXB2 Location RT (249–263)
Author Location (243–263)
Epitope KDSWTVNDIQKLVGK
Epitope name pep23
Immunogen Vaccine

Vector/Type: bacteriophage coat protein, dihydrolipoyl acetyltransferase E2 protein, of Bacillus stearothermophilus *HIV component:* RT
Species (MHC) transgenic mouse (HLA-DR)
Assay type Chromium-release assay
Keywords vaccine antigen design
References De Berardinis *et al.* 2003

- An RT T-helper (KDSWTVNDIQKLVGK) that can be promiscuously presented by multiple HLA-DR molecules, and an RT CTL epitope (ILKEPVHGV) presented by HLA-A2, were displayed using two different antigen presentation systems, bacteriophage virions or E2 protein scaffolds. Both systems enabled display of the epitopes in a mouse model system to the immune system. CTL responses were detected in immunized mice, and were processed correctly for both class I and class II presentation.

HXB2 Location RT (251–261)
Author Location RT (250–260)
Epitope SSTVNDIQKLV
Immunogen in vitro stimulation or selection
Species (MHC) human (DR5(11.01))
References Manca *et al.* 1996

- This peptide was the minimal stimulatory sequence.
- One Th line was stimulated by p66, one by a Glutathione-S-transferase (GST)-peptide fusion protein.
- Constructs linking GST to the KDSSTVNDIQKLVGK peptide at the N-term end of GST stimulated Th cells, but not constructs linking at the C-term end.
- The C and N termini of GST are not intrinsically permissive or non-permissive, presentation is epitope specific (see FAILKCNNK for contrast)

HXB2 Location RT (258–272)
Author Location RT (IIIB)
Epitope QKLWGKLNWASQIYP
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming did not induce T-cells that recognize whole protein.

HXB2 Location RT (271–290)
Author Location RT (271–290 HXB2)
Epitope YPGIKVRQLCKLLRGTKALT
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References van der Burg *et al.* 1999

- Epitope can bind to at least 5 different HLA-DR molecules, and peptide on target cells can elicit Th responses from PBMC cultures from healthy donors, however it does not seem to be processed properly from whole RT or virus.

HXB2 Location RT (271–290)
Author Location RT (271–290 HXB2)
Epitope YPGIKVRQLCKLLRGTKALT
Subtype B
Immunogen HIV-1 infection, in vitro stimulation or selection
Species (MHC) human (DR1, DR2, DR3, DR5, DR7)
Keywords binding affinity, cross-presentation by different HLA
References van der Burg *et al.* 1999

- The goal of this study was to identify Th epitopes that could be cross-presented by multiple class II HLA molecules. 5 RT peptides were identified that could bind to more than one HLA class II protein, but only 2/5 could stimulate strong proliferation responses in PBMC derived from multiple healthy donors.
- This epitope binds with high affinity to HLA-DR1, -DR2, -DR3, -DR5, and -DR7 but not HLA-DR4, and stimulated proliferation in 3/4 individuals with the appropriate HLA alleles.
- This epitope was not able to be naturally processed in protein-pulsed stimulator cells.

HXB2 Location RT (276–290)
Author Location RT (IIIB)
Epitope WRQLCKLLRGTKALT
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Protein priming induced T-cells that recognize peptide.

HXB2 Location RT (285–299)
Author Location RT (IIIB)
Epitope GTKALTEVIPLTEEA
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Protein priming induced T-cells that recognize peptide.

HXB2 Location RT (294–308)
Author Location RT (IIIB)
Epitope PLTEEAELELAENRE
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Protein priming induced T-cells that recognize peptide.

HXB2 Location RT (303–317)
Author Location RT (IIIB)
Epitope LAENREILKEPVHGV
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Protein priming induced T-cells that recognize peptide.

HXB2 Location RT (384–398)
Author Location RT (IIIB)
Epitope GKTPKFKLPIQKETW
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Protein priming induced T-cells that recognize peptide.

HXB2 Location RT (414–428)
Author Location Pol (596–610)
Epitope WEFVNTPPLVKLWYQ

Epitope name Pol 596
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds eleven HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101, with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 84% of clade B isolates.
- 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location RT (414–428)
Author Location RT (596–610)
Epitope WEFVNTPPLVKLWYQ
Epitope name Pol3
Immunogen HIV-1 infection
Species (MHC) human (DR(supermotif))
Country United Kingdom.
Assay type cytokine production, proliferation
Keywords supertype, rate of progression
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.
- Pol3 was 1 of 2 peptides that had a positive correlation between absolute number and percentage of responding cells and viral load. Pol3 responses were also negatively correlated with CD4 counts. In contrast, the absolute number of 3/11 peptides studied were negatively correlated with viral load.

HXB2 Location RT (429–443)
Author Location RT (IIIB)
Epitope LEKEPIVGAETFYVD
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Protein priming induced T-cells that recognize peptide.

HXB2 Location RT (432–450)
Author Location RT (431–450 HXB2)
Epitope EPIVGAETFYVDGAANRET
Subtype B
Immunogen HIV-1 infection, in vitro stimulation or selection
Species (MHC) human (DR1, DR2, DR3, DR4)
Keywords binding affinity, cross-presentation by different HLA
References van der Burg *et al.* 1999

- The goal of this study was to identify Th epitopes that could be cross-presented by multiple class II HLA molecules. 5 RT peptides were identified that could bind to more than one HLA class II protein, and but only 2/5 could stimulate strong proliferation responses in PBMC derived from multiple healthy donors.
- This epitope binds with high affinity to HLA-DR1, -DR2, -DR3, and -DR4, but stimulated a strong proliferation response in only 1/4 individuals tested so was not considered broadly cross-presented.

HXB2 Location RT (526–540)
Author Location RT (526–540 BRU)
Epitope IKKEKVYLAWVPAHK
Epitope name W9
Subtype B
Immunogen Vaccine
Vector/Type: peptide, protein, inactivated HIV *Strain:* B clade BRU *HIV component:* RT, virus *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (Ad or Dd)
References Haas *et al.* 1991

- Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus.
- B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.
- The peptide KEKVYLAWVPAHKG was one of two RT peptides with Th cells recognition.

HXB2 Location RT (528–540)
Author Location RT (528–540)
Epitope KEKVYLAWVPAHK
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade BRU *HIV component:* RT *Adjuvant:* P3CSS
Species (MHC) mouse (H-2b, H-2d, H-2k)
Assay type proliferation
References Loleit *et al.* 1996

- BALB/c, C3H/Hej, and C57BL/6 mice were immunized with 22-mer lipopetide tripeptide conjugates P3CSS-[RT-(522-543)] and P3CSS-[RT-(528-549)] of HIV-1 RT, which included the optimal T-helper epitope [RT-(528-540)]. P3CSS conjugated RT epitopes resulted in a specific Th responses, and mice were primed for secondary recognition of native RT. A proximal B cell epitope was also active, containing the motif EQVD.

HXB2 Location RT (528–541)

Author Location RT (528–543 BRU)
Epitope KEKVYLAWVPAHKG
Epitope name A3
Subtype B
Immunogen Vaccine
Vector/Type: peptide, protein, inactivated HIV *Strain:* B clade BRU *HIV component:* RT, virus *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (Ad and Dd)
Donor MHC H-2d, H-2f, H-2k
References Haas *et al.* 1991

- Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus.
- B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.
- The peptide KEKVYLAWVPAHKG was one of two RT peptides with Th cells recognition. It could by itself prime different strains of mice for RT-specific Th responses, and the C-term half of the peptide is highly conserved in HIV-1, HIV-2 and SIV strains.

HXB2 Location RT (528–543)
Author Location RT (528–543 BRU)
Epitope KEKVYLAWVPAHKGIG
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BRU
Species (MHC) mouse ($H\text{-}2^{f,\,k,\,d}$)
References Haas *et al.* 1991

- T-cells from peptide-primed mice could be restimulated by native RT.

HXB2 Location RT (529–543)
Author Location Pol (711–725)
Epitope EKVYLAWVPAHKGIG
Epitope name Pol 711
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds ten HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101, with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 94% of clade B isolates.
- 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location RT (529–543)
Author Location Protease-RT (711–725)
Epitope EKVYLAWVPAHKGIG
Epitope name Pol4
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Assay type proliferation, Intracellular cytokine staining
Keywords rate of progression, superinfection
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.

HXB2 Location RT (529–543)
Author Location Pol (711–725)
Epitope EKVYLAWVPAHKGIG
Epitope name Pol 711
Immunogen Vaccine
Vector/Type: DNA with CMV promotor, peptide *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (I-Ab and HLA-DR)
Donor MHC H-2b
Keywords vaccine-specific epitope characteristics, immunodominance
References Livingston *et al.* 2002

- Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice.
- Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.
- Although responses to this peptide indicated it was immunodominant, responses to all four peptides were made upon vaccination with linear constructs when GPGPG spacers were used.

HXB2 Location RT (530–544)
Author Location Pol (712–726)
Epitope KVYLAWVPAHKGIGG
Epitope name Pol 712
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds ten HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101, with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 89% of clade B isolates.
- 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location RT (530–544)
Author Location RT (712–726)
Epitope KVYLAWVPAHKGIGG
Epitope name Pol5
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Country United Kingdom.
Assay type proliferation, Intracellular cytokine staining
Keywords supertype, rate of progression
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.
- Pol5 was 1 of 2 peptides that had a positive correlation between absolute number and percentage of responding cells and viral load. In contrast, the absolute number of 3/11 peptides studied were negatively correlated with viral load.

III-B-6 RT-Integrase Helper, CD4+, T-cell epitopes

HXB2 Location RT-Integrase (553–3)
Author Location RT (720–730 LAI)
Epitope SAGIRKVLFLD
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

III-B-7 Integrase Helper, CD4+, T-cell epitopes

HXB2 Location Integrase (16–30)
Author Location Pol (758–772)
Epitope HSNWRAMASDFNLPP
Epitope name Pol 758
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds eight HLA-DR alleles: DRB4*0101, DRB5*0101, DRB1*0901, DRB1*0701, DRB1*1101, DRB1*0405, DRB1*0401 and DRB1*0101, with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 68% of clade B isolates.
- 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location Integrase (16–30)
Author Location Integrase (758–772)
Epitope HSNWRAMASDFNLPP
Epitope name Pol6
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Country United Kingdom.
Assay type proliferation, Intracellular cytokine staining
Keywords supertype, rate of progression
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.
- Pol6 was 1 of 3 peptides that had a negative correlation between absolute number of responding cells and viral load.

HXB2 Location Integrase (172–186)
Author Location RT (899–913 LAI)
Epitope LKTAVQMAVFIHNFK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location Integrase (173–187)
Author Location Pol (915–929)
Epitope KTAVQMAVFFIHNFKR
Epitope name Pol 915
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds seven HLA-DR alleles: DRB5*0101, DRB1*1302, DRB1*1101, DRB1*0405, DRB1*0401, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 94% of clade B isolates.
- 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location Integrase (173–187)
Author Location Integrase (915–929)
Epitope KTAVQMAVFIHNFKR
Epitope name Pol7
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Country United Kingdom.
Assay type proliferation, Intracellular cytokine staining
Keywords supertype, rate of progression, immunoprophylaxis
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.

HXB2 Location Integrase (196–210)
Author Location RT (923–937 LAI)
Epitope AGERIVDIIATDIQT
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location Integrase (214–228)
Author Location Pol (956–970)
Epitope QKQITKIQNFRVYYR
Epitope name Pol 956
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Keywords inter-clade comparisons
References Wilson *et al.* 2001

- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.
- This epitope binds twelve HLA-DR alleles: DRB4*0101, DRB5*0101, DRB1*0901, DRB1*0802, DRB1*0701, DRB1*1302, DRB1*1201, DRB1*1101, DRB1*0405, DRB1*0401, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM.
- This epitope sequence is conserved in 95% of clade B isolates.
- 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

HXB2 Location Integrase (214–228)
Author Location Integrase (956–970)
Epitope QKQITKIQNFRVYYR
Epitope name Pol8
Immunogen HIV-1 infection
Species (MHC) human (DR supermotif)
Country United Kingdom.
Assay type proliferation, Intracellular cytokine staining
Keywords supertype, rate of progression
References Boaz *et al.* 2003

- Proliferative and cytokine (IFNgamma and Il-2) immune responses to 11 previously defined (Wilson 2001), and immunodominant and broadly cross-reactive Th epitopes and to p24 overlapping peptides were characterized in 10 LTNPs (chronically infected, asymptomatic, long term non-progressors, CD4+ T cells >500 after 15 years) and 7 SPs (slow progressors, CD4+ T cell declined to <500 after 15 years. Patients were treatment-naive.
- Gag-specific CD4+ T cells in LTNPs showed increased numbers of IFN gamma and IL-2 producing cells compared to SPs. Cytokine production and proliferative responses were negatively correlated with the viral load and positively correlated with the CD4+ T cell count. IL-2, but not IFNgamma, levels were correlated with proliferation.
- Pol8 was the only peptide that had higher cytokine responses in LTNPs than SPs ($p = 0.0431$). No peptide had detectable differences in proliferative responses between the two groups.

HXB2 Location Integrase (215–227)
Author Location RT (942–954 LAI)
Epitope KQITKIQNFRVYY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location Integrase (250–267)
Author Location Integrase (250–267 B Consensus)
Epitope VIQDNSDIKVVPRRKAKI

Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

III-B-8 Pol Helper, CD4+, T-cell epitopes

HXB2 Location Pol
Author Location Gag/Pol
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Gag, Pol, Vif *Adjuvant:* B7, IL-12
Species (MHC) mouse
References Kim *et al.* 1997b

- A gag/pol DNA vaccine delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12 gives a dramatic increase in both the cytotoxic and proliferative responses in mice.

HXB2 Location Pol
Author Location Gag/Pol
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Gag, gp160, Pol *Adjuvant:* CD86
Species (MHC) mouse
References Kim *et al.* 1997d

- A gag/pol DNA vaccine delivered in conjunction with the plasmid encoding the co-stimulatory molecule CD86 gives an increase in proliferative responses to Pr55 in mice.

HXB2 Location Pol
Author Location Gag/Pol (MN)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade MN *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86
Species (MHC) chimpanzee
References Kim *et al.* 1998

- Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.

HXB2 Location Pol
Author Location Pol
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Blankson *et al.* 2001

- 5/10 chronically HIV infected patients with low CD4+ counts who received HAART therapy and experienced immune reconstitution displayed p24, p17 and p66 T-helper CD4 proliferative responses, in contrast to 0/8 chronically HIV infected patients with high CD4+ counts at the initiation of antiretroviral treatment.
- This surprising result could be due to the low CD4 nadir patients being more likely to have thymic regeneration or a peripheral expansion of T cells.

HXB2 Location Pol
Author Location p66
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.

HXB2 Location Pol
Author Location p66
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Palmer *et al.* 2002

- CD4+ T cell proliferative responses from 33 HIV-1 infected patients with HAART suppression were compared to 19 patients with active viral replication (HAART failures and HAART naive). Patients with HAART suppression showed stronger p24- and p66-specific proliferative responses compared to patient groups with active HIV-1 replication, suggesting active

viral replication *in vivo* specifically reduces proliferation responses.
- No differences in the frequency of HIV-specific CD4+ T-cells that were positive for cytokine secretion in a flow cytometry assay were found in the HAART suppressed group versus the group with active viral replication.

HXB2 Location Pol
Author Location (BRU)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade BRU *HIV component:* RT, virus *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse
References Haas *et al.* 1991
- Of 5 mouse inbred lines tested DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus.
- B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.

HXB2 Location Pol
Author Location RT (248–256 HXB2)
Epitope
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DR5)
References Manca *et al.* 1995b
- CD4+ T-cell lines from uninfected individuals by stimulation with p66-pulsed APC.
- TcR Vβ Dβ Jβ sequences were obtained from p66-specific T-cell clones.
- There were multiple responses to peptides throughout p66, but because of uncertain locations, they have not been mapped.
- Response to peptide 248-256 was associated with DR5.

HXB2 Location Pol
Author Location RT
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol *Adjuvant:* IFNγ, IL-2, IL-4
Species (MHC) mouse (H-2^d)
Keywords Th1
References Kim *et al.* 2000
- Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of Th1 cytokine IFNγ drove Th1 immune responses and enhanced CTL responses.

HXB2 Location Pol
Author Location RT
Epitope
Immunogen Vaccine
Vector/Type: Salmonella *HIV component:* RT
Species (MHC) mouse (H-2^d)
References Burnett *et al.* 2000
- A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV RT gene in the Lpp-OmpA-HIV fusion protein, induced a lymphoproliferative Th response in BALB/c mice.

III-B-9 Vif Helper, CD4+, T-cell epitopes

HXB2 Location Vif (65–76)
Author Location Vif (65–80)
Epitope VITTYWGLHTGE
Immunogen HIV-1 infection
Species (MHC) human
References Ranki *et al.* 1997
- T-cell response to this epitope persisted after seroreversion.

HXB2 Location Vif (81–96)
Author Location Vif (81–96)
Epitope LGQGVSIEWRKQRYST
Immunogen HIV-1 infection
Species (MHC) human
References Ranki *et al.* 1997
- T-cell response to this epitope persisted after seroreversion.

HXB2 Location Vif
Author Location Vif
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Vif, Vpu
Species (MHC) mouse (H-2^d)
Keywords inter-clade comparisons, Th1
References Ayyavoo *et al.* 2000
- Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFNγ levels.
- Antigen stimulation increased IFNγ production in pVVN-P immunized mice, indicating a Th1 response.
- IL-4 production was not significantly changed after antigen stimulation compared to control levels.
- Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.

III-B-10 Vpr Helper, CD4+, T-cell epitopes

HXB2 Location Vpr (66–80)
Author Location Vpr (66–80 IIIB)
Epitope QLLFIHFRIGCRHSR
Immunogen HIV-1 infection
Species (MHC) human
References Sarobe *et al.* 1994

- This peptide was found to stimulate proliferative responses in 37.5% of HIV-1 positive individuals.

HXB2 Location Vpr (66–80)
Author Location Vpr (66–80 IIIB)
Epitope QLLFIHFRIGCRHSR
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-2^d)
References Sarobe *et al.* 1994
- Included as a Th stimulatory component of peptide vaccines that also incorporated B-cell epitopes.

III-B-11 Tat Helper, CD4+, T-cell epitopes

HXB2 Location Tat (1–20)
Author Location Tat (1–20 LAI)
Epitope MEPVDPRLEPWKHPGSQPKT
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997
- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Tat (16–35)
Author Location Tat (16–35 LAI)
Epitope SQPKTACTTCYCKKCCFHCQ
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997
- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Tat (17–32)
Author Location Tat (17–32)
Epitope QPKTACTNCYCKRCCF
Immunogen HIV-1 infection
Species (MHC) human
References Ranki *et al.* 1997
- T-cell response to this epitope persisted after seroreversion.

HXB2 Location Tat (17–32)
Author Location Tat (17–32 HXB2)
Epitope QPKTACTNCYCKKCCF
Epitope name D26
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DR5? plus others)
Keywords immunodominance
References Blazevic *et al.* 1993
- 9/14 (64%) of HIV-1 positive patients had proliferative T-cell responses associated with IL-2 production against at least one Tat-derived synthetic peptides of twelve overlapping 15-16 mer peptides spanning Tat. T cell proliferation was associated with IL-2 production.
- 3/12 peptides were recognized.
- This immunodominant, highly conserved and most frequently recognized peptide was recognized by 57% of the HIV-1 infected patients. A beta-sheet secondary structure was predicted at aa residues 21-28, but no amphipathic helix structure, suggested to be most favorable for T-cell epitopes, was indicated.
- This peptide contained epitopes restricted by several HLA DR alleles, although the frequency of DR5 was enriched (3/6) among the patients that recognized the peptide.

HXB2 Location Tat (31–50)
Author Location Tat (31–50 LAI)
Epitope CFHCQVCFTTKALGISYGRK
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997
- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Tat (33–48)
Author Location Tat (33–48)
Epitope HCQVCFMTKGLGISYG
Immunogen HIV-1 infection
Species (MHC) human
References Ranki *et al.* 1997
- T-cell response to this epitope persisted after seroreversion.

HXB2 Location Tat (33–48)
Author Location Tat (33–48 HXB2)
Epitope HCQVCFITKALGISYG
Epitope name D28
Immunogen HIV-1 infection
Species (MHC) human (DR5? plus others)
References Blazevic *et al.* 1993
- 9/14 (64%) of HIV-1 positive patients had proliferative T-cell responses associated with IL-2 production against at least one Tat-derived synthetic peptides of twelve overlapping 15-16 mer peptides spanning Tat. T cell proliferation was associated with IL-2 production.
- 3/12 peptides were recognized.
- 4/14 HIV+ people recognized this peptide.
- An alpha-helix structure was predicted at residues 39-44, but charge patterns did not indicate it was an amphipathic helix, suggested to be most favorable for T-cell epitopes.

- This peptide contained epitopes restricted by several HLA DR alleles, although the frequency of DR5 was enriched (2/4) among the patients that recognized the peptide.

HXB2 Location Tat (36–50)
Author Location Tat (36–50 HTLV IIIB)
Epitope VCFITKALGISYGRK?
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2)
Species (MHC) mouse (H-2^d)
Assay type cytokine production, proliferation, T-cell Elispot, Th support of CTL response
Keywords Th1, Th2, mucosal immunity
References Borsutzky *et al.* 2003

- BALB/c mice that were vaccinated intranasally with Tat protein plus mucosal adjuvant macrophage-activating lipopeptide-2 (MALP-2) had increased proliferative, antibody, and IFNγ producing T-cell responses than did with Tat+IFA delivered by the i.p. route.
- IFA as adjuvant stimulated a Th2-dominant response pattern, and MALP-2 as adjuvant shifted to a Th1 response. Anti-Tat IgG1 dominated the Ab response with IFA, IgG2b dominated with MALP-2. In animals vaccinated with Tat+MALP-2, IFNγ and IL-2 were the most prominent cytokines, with some IL-6. In contrast, in mice vaccinated with Tat+IFA, IL-6 was the dominant cytokine. Secreted IL-4, IL-5 and IL-10 were below the detection limit in both cases.
- The strongest proliferation of spenocytes was observed was after re-stimulation with residues 36-50 and 56-70.

HXB2 Location Tat (41–50)
Author Location Tat (40–50 C consensus)
Epitope KGLGISYGRK?
Subtype C
Immunogen Vaccine
Vector/Type: DNA *Strain:* C clade consensus *HIV component:* Tat *Adjuvant:* ubiquitin
Species (MHC) mouse
Donor MHC H-2d
Assay type proliferation, CD4 T-cell Elispot - IFNγ
Keywords Th1, vaccine antigen design
References Ramakrishna *et al.* 2004

- BALB/c and C57BL/6 mice were intramuscularly immunized with a codon optimized HIV-1 C-consensus Tat DNA vaccine that was linked to ubiquitin to facilitate rapid processing. Ubiquitin and codon optimization enhanced Th1 T cell responses, with increased proliferative responses, cytotoxic responses, and Th1 responses measured by IFNgamma EliSpot, but not the Th2 responses, measured by IL-4 EliSpot..
- Several immunogenic regions in HIV-1 Tat were identified in BALB/c mice using EliSpot. The strongest immune response was within the core region of Tat; the peptides based on the C subtype consensus positions 30-50 and 40-60 gave the strongest EliSpot responses in BALB/c mice, suggesting a putative helper T-cell epitope spanning the region of overlap, residues 40-50.

HXB2 Location Tat (46–65)
Author Location Tat (46–65 LAI)
Epitope SYGRKKRRQRRRPPQGSQTH
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Tat (56–70)
Author Location Tat (56–70 HTLV IIIB)
Epitope RRAHQNSQTHQASLS?
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2)
Species (MHC) mouse (H-2^d)
Assay type cytokine production, proliferation, T-cell Elispot, Th support of CTL response
Keywords Th1, Th2
References Borsutzky *et al.* 2003

- BALB/c mice that were vaccinated intranasally with Tat protein plus mucosal adjuvant macrophage-activating lipopeptide-2 (MALP-2) had increased proliferative, antibody, and IFNγ producing T-cell responses than did with Tat+IFA delivered by the i.p. route.
- IFA as adjuvant stimulated a Th2-dominant response pattern, and MALP-2 as adjuvant shifted to a Th1 response. Anti-Tat IgG1 dominated the Ab response with IFA, IgG2b dominated with MALP-2. In animals vaccinated with Tat+MALP-2, IFNγ and IL-2 were the most prominent cytokines, with some IL-6. In contrast, in mice vaccinated with Tat+IFA, IL-6 was the dominant cytokine. Secreted IL-4, IL-5 and IL-10 were below the detection limit in both cases.
- The strongest proliferation of spenocytes was observed was after re-stimulation with residues 36-50 and 56-70.

HXB2 Location Tat (61–80)
Author Location Tat (61–80 LAI)
Epitope GSQTHQVSLSKQPTSQPRGD
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally; rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Tat (65–80)
Author Location Tat (65–80 HXB2)
Epitope HQASLSKQPTSQPRGD
Epitope name D32
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DR2? plus others)
References Blazevic *et al.* 1993

- 9/14 (64%) of HIV-1 positive patients had proliferative T-cell responses associated with IL-2 production against at least one Tat-derived synthetic peptides of twelve overlapping 15-16 mer peptides spanning Tat. T cell proliferation was associated with IL-2 production.
- 3/12 Tat peptides were recognized.
- 3/14 HIV+ people recognized this peptide.
- An alpha-helix structure was predicted at residues 65-72, but charge patterns did not indicate it was an amphipathic helix, suggested to be most favorable for T-cell epitopes..
- This peptide contained epitopes restricted by several HLA DR alleles, although the frequency of DR2 was enriched (2/3) among the patients that recognized the peptide.

HXB2 Location Tat (67–86)
Author Location Tat (67–86 LAI)
Epitope VSLSKQPTSQPRGDPTGPKE
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat
Species (MHC) human
Keywords HAART, ART
References Calarota *et al.* 1999

- 9/9 HIV-1 + subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated.
- The nef DNA immunization induced the highest and most consistent CTLp activity, IFNγ production, and IL-6 and IgG responses.
- Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS)
Species (MHC) human
Keywords review, Th1
References Calarota & Wahren 2001

- This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen in vitro stimulation or selection
Species (MHC) human
Keywords dendritic cells, Th1, Th2
References Corinti *et al.* 2002

- In vitro delivery of recombinant Tat protein conjugated to red blood cells (RBCs) via avidin-biotin bridges (RBC-Tat) to human dendritic cells was compared to dendritic cells pulsed with rec Tat.
- Dendritic cells pulsed with RBC-Tat elicited specific and significantly stronger CD4+ and CD8+ T-cell responses and required 1250-fold less antigen than DCs stimulated with soluble Tat.
- Dendritic cells which were maturated in the presence of IFNgamma induced elevated IL-12 and TNF-alpha secretion. IFNgamma upregulated IP-10 and down regulated TARC, chemokines which attract Th1 and Th2 cells, respectively.

HXB2 Location Tat
Author Location Tat (IIIB, BH10)
Epitope
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human
Keywords epitope processing, vaccine-specific epitope characteristics, dendritic cells, Th1
References Fanales-Belasio *et al.* 2002b

- Biologically active HIV-1 Tat is readily taken up by monocyte-derived dendritic cells (MDDC) (and activated endothelial cells), but not other APCs. Tat must be in a native, non-oxidized conformation for efficient uptake. Tat upregulates MHC molecules, IL-12, TNFα, RANTES and MIP-1-α and MIP-1-β production which drives Th1 immune responses and enhances antigen presentation.
- Native Tat enhanced the antigen presentation of MDDC and boosted proliferative recall and allogeneic antigen responses, and the authors propose it could be used as an adjuvant to drive the immune response as well as an antigen.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen Vaccine
Vector/Type: DNA, protein *HIV component:* Tat *Adjuvant:* aluminum hydroxide, Ribi adjuvant (MPL+TDM) (RIBI)

Species (MHC) macaque
Assay type cytokine production, Delayed-type hypersensitivity (DTH)
Keywords review, early-expressed proteins, Th1
References Fanales-Belasio *et al.* 2002a

- HIV-1 Tat protein has several virtues vaccine component. It is an early expressed protein, and though variable, contains consverved T-cell and B-cell epitopes that allow cross-clade recognition. It is efficiently taken up by monocyte-derived dendritic cells (MDDCs) and in this context can stimulate Th1 immune responses. A Tat based vaccine can elicit an immune response that can control primary infection in monkeys that are in early stage of in infection with SHIV89.6P.

HXB2 Location Tat
Author Location Tat (1–72)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: protein, nanoparticle *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* aluminum hydroxide, lipid A
Species (MHC) mouse
Donor MHC H-2d
Assay type cytokine production, proliferation
Keywords Th1, Th2, adjuvant comparison, vaccine antigen design
References Cui *et al.* 2004

- Mice were subcutaneously injected on day 0 and 14 with either Alum and Tat (Th2 control) or Lipid A-adjuvanted Tat (Th1 control), or Tat coated anionic nanoparticles. Analysis of Ab and cytokine release in splenocytes (day 28) showed both IgG and IgM Ab responses; immunization with Tat-coated nanoparticles induced a Th1-biased immune response.
- IFN gamma responses were 3.3-fold stronger with Tat and either Lipid-A or coated nanoparticles than with Tat and Alum.

HXB2 Location Tat
Author Location Tat
Epitope
Immunogen Vaccine
Vector/Type: DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18
Species (MHC) mouse (H-2^d)
Keywords Th1, Th2
References Billaut-Mulot *et al.* 2001

- DNA vaccinated BALB/c mice primed and boosted with a multiepitopic vaccine with IL18 gave lymphoproliferative responses 7 weeks post immunization.
- Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime + DNA boost was more effective than DNA prime + protein boost.
- Immunization with either the multiepitopic DNA or with the mixed DNA vaccine resulted in Th1 cytokines production (IL-2 and IFNγ) in spleen cell cultures stimulated by Tat and Gag, while Th2 cytokines IL-4 and IL-10 production was not detectable.
- Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.

III-B-12 Rev Helper, CD4+, T-cell epitopes

HXB2 Location Rev (9–23)
Author Location Rev (9–23 HXB2)
Epitope DEELIRTVRLIKLLY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Blazevic *et al.* 1995

- One of four peptides that stimulates in PBLs from HIV-1 + donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated.

HXB2 Location Rev (14–30)
Author Location Rev (14–30 B Consensus)
Epitope KTVRLIKFLYQSNPPPS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location Rev (16–35)
Author Location Rev (16–35 LAI)
Epitope VRLIKFLYQSNPPPNPEGTR
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.

- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Rev (25–39)
Author Location Rev (25–39 HXB2)
Epitope SNPPPNPEGTRQARR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Blazevic *et al.* 1995

- One of four peptides that stimulates in PBLs from HIV-1 + donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated.

HXB2 Location Rev (31–50)
Author Location Rev (31–50 LAI)
Epitope PEGTRQARRNRRRRWRERQR
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Rev (33–48)
Author Location Rev (33–48 HXB2)
Epitope GTRQARRNRRRRWRER
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Blazevic *et al.* 1995

- One of four peptides that stimulates in PBLs from HIV-1 + donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated.

HXB2 Location Rev (41–56)
Author Location Rev (41–56 HXB2)
Epitope RRRRWRERQRQIHSIS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Blazevic *et al.* 1995

- One of four peptides that stimulates in PBLs from HIV-1 + donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated.

HXB2 Location Rev (76–95)
Author Location Rev (76–95 LAI)
Epitope PPLERLTLDCNEDCGTSGTQ
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^b)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Rev (96–116)
Author Location Rev (96–116 LAI)
Epitope GVGSPQILVESPTVLESGTKE
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Rev
Species (MHC) mouse
Keywords HAART, ART
References Chan *et al.* 1998

- Rev M10 is a construct that was introduced into mice through a genetic vaccination.
- Rev was used to test for down-regulation of HIV-1 in infected cells as a method for gene therapy – in the course of this study, Rev-specific IL-2 producing Th cells developed in the mice.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat
Species (MHC) human
Keywords HAART, ART
References Calarota *et al.* 1999

- 9/9 HIV-1 + subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated.
- The nef DNA immunization induced the highest and most consistent CTLp activity, IFNγ production, and IL-6 and IgG responses.
- Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen HIV-1 infection, Vaccine

Vector/Type: DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS)
Species (MHC) human
Keywords review, Th1
References Calarota & Wahren 2001

- This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals.

HXB2 Location Rev
Author Location Rev
Epitope
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade MN *HIV component:* Env, Rev *Adjuvant:* Bupivacaine
Species (MHC) human
Keywords early-expressed proteins
References MacGregor *et al.* 2002

- A phase I clinical trial of a HIV-1 Env and Rev DNA vaccine with a CMV promoter was conducted and Th proliferative, CTL and Elispot responses monitored. The construct was modified for safety and included no LTRs or packaging signals. The vaccine strategy was safe, and elicited strong CD4-T cell responses, but not CD8 T-cell responses. Rev elicited strong Th responses, and is a early produced protein so may confer advantages.
- With a 300 ug dose, 4/6 individuals had a lymphocyte proliferation (LP) responses to gp120, 3/6 to Rev.
- With a 1000 ug dose, 4/6 individuals had a LP and 2/6 had IFNgamma Elispot responses to gp160; 3/6 had LP, and 4/6 had IFNgamma Elispot responses to Rev.
- No responses to three specific CTL epitopes were observed by Elispot in individuals with appropriate HLA. Some cytotoxic activity against whole protein was observed that was CD4+ T-cell mediated.

III-B-13 Vpu Helper, CD4+, T-cell epitopes

HXB2 Location Vpu (19–34)
Author Location Vpu (19–34)
Epitope AIVVWSIVLIEYRKIL
Immunogen HIV-1 infection
Species (MHC) human
References Ranki *et al.* 1997

- T-cell response to this epitope persisted after seroreversion.

HXB2 Location Vpu
Author Location Vpu
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Vif, Vpu
Species (MHC) mouse (H-2^{d})
Keywords inter-clade comparisons, Th1
References Ayyavoo *et al.* 2000

- Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFNγ levels.
- Antigen stimulation increased IFNγ production in pVVN-P immunized mice, indicating a Th1 response.
- IL-4 production was not significantly changed after antigen stimulation compared to control levels.
- Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.

III-B-14 gp160 Helper, CD4+, T-cell epitopes

HXB2 Location gp160 (30–51)
Author Location gp120 (30–51 IIIB)
Epitope ATEKLWVTVYYGVPVWKEATTT?
Epitope name A1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 2/15 responders recognized this peptide, mean SI = 4.6.

HXB2 Location gp160 (32–44)
Author Location gp120 (39–51)
Epitope EQLWVTVYYGVPV
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-2^{bxk})
References Sastry & Arlinghaus 1991

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160.

HXB2 Location gp160 (38–48)
Author Location Env (45–55)
Epitope VYYGVPVWKEA
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) macaque
References Nehete *et al.* 1993

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice.
- Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys.

HXB2 Location gp160 (38–48)
Author Location Env (45–55)
Epitope VYYGVPVWKEA
Immunogen HIV-1 infection
Species (MHC) human, chimpanzee
References Nehete *et al.* 1998b

- Seven out of nine HIV-infected chimpanzees and eight out of seventeen HIV-positive humans exhibited positive proliferative responses to this conserved peptide (peptide 104) – no HIV negative individuals showed a response.
- This peptide, along with 4 other peptides from conserved regions of envelope, can induce proliferative responses to HIV and may be useful for vaccines.
- Peptide 104 elicited proliferative responses in inbred mouse strains and outbred rhesus monkeys in previous study by same group.

HXB2 Location gp160 (38–48)
Author Location gp120 (45–55)
Epitope VYYGVPVWKEA
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-$2^{bxk, sxd}$)
References Sastry & Arlinghaus 1991

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160.

HXB2 Location gp160 (41–54)
Author Location Env (48–60)
Epitope GVPVWKEATTLFC
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) macaque
References Nehete *et al.* 1993

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice.
- Despite the proliferative response to this peptide in mice, no response was observed in 3 rhesus monkeys.

HXB2 Location gp160 (41–54)
Author Location gp120 (48–61)
Epitope GVPVWKEATTLFC
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-2^{sxd})
References Sastry & Arlinghaus 1991

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160.

HXB2 Location gp160 (41–60)
Author Location gp120 (40–59 89.6)
Epitope GVPVWREATTTLFCASDAKA
Epitope name Peptide 2
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was highly reactive in 10/10 BALB/c mice tested, but only in 5/10 CBA/J mice.

HXB2 Location gp160 (41–60)
Author Location gp120 (40–59 89.6)
Epitope GVPVWREATTTLFCASDAKA
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse (H-2^{d})
Keywords immunodominance
References Dai *et al.* 2001

- Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^{k} and BALB/c H-2^{d} mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence.
- This peptide was recognized by 10/10 BALB/c with an average SI of 6.4, the strongest reaction among BALB/c mice, but not by CBA/J mice, but recognized well not by CBA/J mice, so is considered to be uniquely immunodominant for H-2^{d}
- Uniquely immunodominant sequences tended to be in the inner domain of the protein.

HXB2 Location gp160 (42–61)
Author Location gp120 (42–61 IIIB)
Epitope VPVWKEATTTLFCASDAKAY?
Epitope name A2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 2/15 responders recognized this peptide, mean SI = 6.6.

HXB2 Location gp160 (52–71)
Author Location gp120 (52–71 IIIB)
Epitope LFCASDAKAYDTEVHNVWAT?
Epitope name A3
Subtype B
Immunogen HIV-1 infection

Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 3/15 responders recognized this peptide, mean SI = 4.3.

HXB2 Location gp160 (61–80)
Author Location gp120 (60–79 89.6)
Epitope YDTEVHNVWATHACVPTDPN
Epitope name Peptide 4
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was highly reactive in 4/10 BALB/c mice tested, but only in 1/10 CBA/J mice.

HXB2 Location gp160 (62–80)
Author Location gp120 (62–80 IIIB)
Epitope DTEVHNVWATHACVPTDPN?
Epitope name A4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 3.5.

HXB2 Location gp160 (62–81)
Author Location gp120 (MN)
Epitope DTEVHNVWATQACVPTDPNP
Epitope name DP20
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DR)
Assay type cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords HAART, ART, acute infection, cross-presentation by different HLA
References Malhotra *et al.* 2003

- 92 acute- or early-HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy.
- This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail. The CD4+ clones showed MHC-restricted cytotoxicity and secreted high levels of cytokines when stimulated. These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintained in Env.
- This peptide showed bound to HLA-DRB1*0101.

HXB2 Location gp160 (65–75)
Author Location gp120 (72–82)
Epitope AHKVWATHACV
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-$2^{bxk, sxd}$)
References Sastry & Arlinghaus 1991

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160.

HXB2 Location gp160 (74–85)
Author Location gp120 (74–85 LAI)
Epitope CVPTDPNPQEVV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (74–85)
Author Location gp120 (81–92)
Epitope CVPTNPVPQEVV
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-$2^{bxk, sxd}$)
References Sastry & Arlinghaus 1991

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160.

HXB2 Location gp160 (80–99)
Author Location gp120 (51–70 HXB2)
Epitope NPQEVVLVNTENFNMWKND

Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human
Keywords TCR usage
References Li Pira *et al.* 1998

- Clonal heterogeneity was broad for a recall response to tetanus toxoid or PPD, but oligoclonal to primary HIV antigens, dominated in this case by TCR Vβ 13 usage.
- Donor of PBMC that recognized this epitope had HLA-DR alleles 2 and 7.

HXB2 Location gp160 (81–100)
Author Location gp120 (80–99 89.6)
Epitope PQEVVLGNVTENFNMWKNNM
Epitope name Peptide 6
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was not reactive in any BALB/c mice tested (0/10), but was highly reactive in all (10/10) CBA/J mice.

HXB2 Location gp160 (81–100)
Author Location gp120 (80–99 89.6)
Epitope PQEVVLGNVTENFNMWKNNM
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse (H-2^k)
Keywords immunodominance
References Dai *et al.* 2001

- Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence.
- This peptide was recognized by 10/10 CBA/J with an average SI of 8.2, and not by BALB/c mice, so is considered to be uniquely immunodominant for H-2^k
- Uniquely immunodominant sequences tended to be in the inner domain of the protein.

HXB2 Location gp160 (81–101)
Author Location gp120 (81–101 IIIB)
Epitope PQEVVLVNVTENFNMWKNDMV?
Epitope name B1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 2/15 responders recognized this peptide, mean SI = 5.1.

HXB2 Location gp160 (92–101)
Author Location gp120 (90–100 W6.ID)
Epitope YFNMWKNNMV
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21
Species (MHC) human
References Jones *et al.* 1999

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated.
- One T-cell clone reacts with two overlapping peptides, and the region of overlap is: YFNMWKNNMV.
- The first 20-mer peptide that this clone reacts with is PQEVVLGNVTEYFNMWKNNMV, and the IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version: IIIB: pqevvlVnvteNfDmwknDmv.

HXB2 Location gp160 (92–111)
Author Location gp120 (92–111 W6.ID)
Epitope YFNMWKNNMVDQMHEDIISL
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21
Species (MHC) human
References Jones *et al.* 1999

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated.
- The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide NfDmwknDmvEqmhediisl.
- Six T-cell lines react with this peptide, but some of these can also be stimulated by other gp120 peptides located in different regions of gp120.

HXB2 Location gp160 (101–126)
Author Location gp120 (101–126)
Epitope VEQMHEDIISLWDQSLKPCVKLTPLC
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (MHC) mouse (H-2^k)

References Sjolander *et al.* 1996

- Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein.

HXB2 Location gp160 (102–114)
Author Location gp120 (109–121)
Epitope EQMHEDIISLWDQ
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-2^{bxk})
References Sastry & Arlinghaus 1991

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160.

HXB2 Location gp160 (102–116)
Author Location gp120 (109–123 IIIB)
Epitope EQMHEDIISLWDQSL
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) mouse (H-$2^{d, i5}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (102–116)
Author Location gp160 (109–123 IIIB)
Epitope EQMHEDIISLWDQSL
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^{d}, H-2^{b})
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- B10.D2 (H-$2A^{d}$, E^{d}) and B10.A(R5) (H-$2A^{b}$, E^{b}) mice immunized with rec gp160 showed a proliferative response to EQMHEDIISLWDQSL.
- EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes including HEDIISLWDQSLK and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (102–121)
Author Location gp120 (102–121 IIIB)
Epitope EQMHEDIISLWDQSLKPCVK?
Epitope name B3
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 5.9.

HXB2 Location gp160 (102–121)
Author Location gp160 (109–128 IIIB)
Epitope EQMHEDIISLWDQSLKPCVK
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) human, mouse (H-2^{k}, H-2^{s})
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide.
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people.
- This cluster peptide elicited proliferative responses in cells from vaccinated B10.BR mice (H-$2A^{k}$, E^{k}) and B10.S(9R) mice (H-$2A^{s}$, E^{s}), while shorter peptides from within this region stimulated H-2^{k}, H-2^{d} and H-2^{b} responses, but not H-2^{s}
- IL-2 production was observed in response to this peptide in 64% (23/36) of asymptomatic HIV-infected individuals.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1997

- Used in a study of pentoxifylline's influence on HIV specific T-cells.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 BH10)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) human
References Berzofsky *et al.* 1988

- Proliferative response to T1 and T2 peptides in 14 immunized, uninfected humans.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1989

- IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen HIV-1 infection
Species (MHC) human

References Clerici *et al.* 1991a

- Peptides stimulate Th cell function and CTL activity in similar patient populations.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) human
References Clerici *et al.* 1991b

- Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen
Species (MHC) human
References Clerici *et al.* 1992

- Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen Vaccine
Vector/Type: peptide prime with protein boost
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) macaque
References Hosmalin *et al.* 1991

- Peptide priming to induce T-cell help enhances antibody response to gp160 immunization.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen
Species (MHC) human
References Pinto *et al.* 1995

- CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen HIV-1 infection
Species (MHC) human
References Kaul *et al.* 1999

- Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases)
- Helper epitopes used in this study were noted to be previously described Clerici *et al.* [1989], and were not explicitly described in Kaul *et al.* [1999]

HXB2 Location gp160 (105–117)
Author Location gp120
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human
Keywords inter-clade comparisons, responses in children, mother-to-infant transmission
References Kuhn *et al.* 2001a

- In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4.
- The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents.
- 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breastfeeding.
- Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.

HXB2 Location gp160 (105–117)
Author Location Env (112–124 IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Subtype B
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
Keywords mother-to-infant transmission
References Clerici *et al.* 1993a

- Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected.
- PBL from 10/21 of the mothers showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.

HXB2 Location gp160 (105–117)
Author Location Env (IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC)

Assay type cytokine production
References Clerici *et al.* 1994a

- Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection.
- Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.

HXB2 Location gp160 (105–117)
Author Location HIV-1 (IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Subtype B
Immunogen HIV-1 infection
Species (MHC)
Assay type cytokine production
References Clerici *et al.* 1994b

- IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.

HXB2 Location gp160 (105–117)
Author Location Env (112–124)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen HIV-1 infection
Species (MHC) human
Assay type proliferation
Keywords responses in children, mother-to-infant transmission
References Kuhn *et al.* 2001b

- T helper proliferative responses in cord blood at delivery to a cocktail of HIV envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery.
- The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).

HXB2 Location gp160 (105–117)
Author Location Env (gp160) (105–117)
Epitope HEDIISLWDQSLK
Epitope name TH2
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Country South Africa.
Assay type proliferation
Keywords responses in children, variant cross-recognition or cross-neutralization
References Meddows-Taylor *et al.* 2004

- Viral isolates (gp160) from 16 vertically HIV-1 infected children (8 T-helper cell Env responders and 8 non-responders) were analyzed for variation after comparison with Env peptide sequences (conserved regions T1, T2 and TH4.1, hypervariable regions P18 MN and P181 IIIB) used for in vitro stimulation.
- T2 was the most conserved of the 5 peptides studied.
- No correlation between the age, clinical category (mild or severe), HIV-1 viral load and the degree of epitope variation was established.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 BH10)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen computer prediction
Species (MHC) mouse (H-$2^{k, s}$)
References Cease *et al.* 1987

- 1 of 2 functional epitopes identified using an amphipathic helix epitope prediction algorithm.

HXB2 Location gp160 (105–117)
Author Location gp120 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Epitope name T2
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2^{k})
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (105–117)
Author Location gp160 (112–124 IIIB)
Epitope HEDIISLWDQSLK
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^{k})
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- B10.BR (H-$2A^{k}$, E^{k}) mice immunized with rec gp160 showed a strong proliferative response to three overlapping peptides, QMHEDIISLWDQSL, HEDIISLWDQSLK, and DIISLWDQSLKPCVK, and HEDIISLWDQSLK is common to between them.
- EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes including HEDIISLWDQSLK and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (105–123)
Author Location gp120 (112–130 IIIB)
Epitope HEDIISLWDQSLKPCVKLT
Immunogen
Species (MHC) human
References Furci *et al.* 1997

- 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but none reacted with this previously defined epitope.

HXB2 Location gp160 (108–119)
Author Location gp120 (108–119 LAI)
Epitope IISLWDQSLKPC
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (110–125)
Author Location gp120 (110–125)
Epitope SLWDQSLKPCVKLTPL
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Caruso *et al.* 1997

- As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71.
- The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost.
- This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24.

HXB2 Location gp160 (111–123)
Author Location gp120 (118–130)
Epitope LWDQSLKPCVKLT
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) macaque
References Nehete *et al.* 1993

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice.
- Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys.

HXB2 Location gp160 (112–130)
Author Location gp120 (112–130 IIIB)
Epitope WDQSLKPCVKLTPLCVSLK?
Epitope name B4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 3/15 responders recognized this peptide, average SI = 4.4.

HXB2 Location gp160 (112–141)
Author Location gp120 (112–141 NL43)
Epitope WDQSLKPCVKLTPLCVSLKCTDLGNATNTN
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43
HIV component: gp120, gp160
Species (MHC) human
References Sitz *et al.* 1999

- There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients.
- Over 35% of vaccinees had a stimulation index of greater than 5 to this peptide.

HXB2 Location gp160 (115–126)
Author Location gp120 (115–126 LAI)
Epitope SLKPCVKLTPLC
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (115–129)
Author Location gp120 (115–129 LAI)
Epitope SLKPCVKLTPLCVSL
Subtype B
Immunogen Peptide-HLA interaction
Species (MHC) human (HLA-DR)
Keywords binding affinity
References Gaudebout *et al.* 1997

- Peptide bound to both HLA-DR*1101 and HLA-DR*0401 with high affinity.
- Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding.

HXB2 Location gp160 (121–140)
Author Location gp120 (120–139 89.6)
Epitope KLTPLCVTLNCTNLNITKNT
Epitope name Peptide 10
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6
HIV component: gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal

segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was highly reactive in 5/10 BALB/c mice tested, but not in and (0/10) CBA/J mice.

HXB2 Location gp160 (121–141)
Author Location gp120 (131–151 IIIB)
Epitope KLTPLCVSLKCTDLKNDTNTN?
Epitope name C1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994
- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 3/15 responders recognized this peptide, average SI = 3.9.

HXB2 Location gp160 (122–141)
Author Location gp120 (121–140 MN)
Epitope LTPLCVTLNCTDLRNTTNTN
Epitope name 1931
Subtype B
Immunogen Vaccine
Vector/Type: DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) guinea pig
Keywords vaccine-specific epitope characteristics, Th1
References Chattergoon *et al.* 2002
- Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.
- A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.
- 3/5 animals vaccinated with rec gp120 responded by DTH to this peptide, while 0/6 vaccinated with plasmid gp120 DNA responded.

HXB2 Location gp160 (122–141)
Author Location gp120 (122–141 IIIB)
Epitope LTPLCVSLKCTDLKNDTNTN?
Epitope name B5
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994
- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- 1/15 responders recognized this peptide, SI = 3.1.

HXB2 Location gp160 (136–155)
Author Location gp120 (141–160 MN)
Epitope NSTAWNNSNSEGTIKGGEMK
Epitope name 1932
Subtype B
Immunogen Vaccine
Vector/Type: DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) guinea pig
Keywords vaccine-specific epitope characteristics, Th1
References Chattergoon *et al.* 2002
- Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.
- A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.
- 4/5 animals vaccinated with rec gp120 responded by DTH to this peptide, as did 2/6 vaccinated with plasmid gp120 DNA.

HXB2 Location gp160 (138–159)
Author Location gp120 (141–160 W6.ID)
Epitope TTSNGWTGEIRKGEIKNCSF
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21
Species (MHC) human
References Jones *et al.* 1999
- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated.
- The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide: IIIB: ttsnSSGRMIMEgeiknc sf.

HXB2 Location gp160 (142–161)
Author Location gp120 (142–161 IIIB)
Epitope SSSGRMIMEKGEIKNCSFNI?
Epitope name C2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops.
- 4/15 responders recognized this immunodominant peptide, average SI = 4.3.

HXB2 Location gp160 (147–168)
Author Location gp120 (152–173 NL43)
Epitope MMMEKGEIKNCSFNISTSIRGK
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43
HIV component: gp120, gp160
Species (MHC) human
References Sitz *et al.* 1999

- There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients.
- Over 50% of vaccinees had a stimulation index of greater than 5 to this peptide.

HXB2 Location gp160 (152–171)
Author Location gp120 (152–171 IIIB)
Epitope GEIKNCSFNISTSIRGKVQK?
Epitope name C3
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops.
- 4/15 responders recognized this immunodominant peptide, average SI = 4.4.

HXB2 Location gp160 (155–169)
Author Location Env (UG92005)
Epitope KNCSFNITTELIDKK
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V2 region of UG92005 (UG, clade D) and the hybridoma that recognized it used Vβ5.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (155–169)
Author Location gp120 (160–174 LAI)
Epitope KNCSFNISTSIRGKV
Subtype B
Immunogen
Species (MHC) human (HLA-DR)
Keywords binding affinity
References Gaudebout *et al.* 1997

- Peptide binds to both HLA-DR*1101 and HLA-DR*0401 with high affinity.
- Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding.

HXB2 Location gp160 (159–178)
Author Location gp120 (160–179 89.6)
Epitope FYITTSIRNKVKKEYALFNR
Epitope name Peptide 14
Immunogen Vaccine

Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was highly reactive in 6/10 BALB/c mice tested, and in 4/10 CBA/J mice.

HXB2 Location gp160 (162–181)
Author Location gp120 (162–181 IIIB)
Epitope STSIRGKVQKEYAFFYKLDI
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* Env
Species (MHC) macaque
References Lekutis *et al.* 1997

- HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkeys.

HXB2 Location gp160 (162–182)
Author Location gp120 (162–182 IIIB)
Epitope STSIRGKVQKEYAFFYKLDII?
Epitope name C4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 3.3.

HXB2 Location gp160 (166–185)
Author Location gp120 (MN)
Epitope RDKMQKEYALLYKLDIVSID
Epitope name RD20
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords HAART, ART, acute infection
References Malhotra *et al.* 2003

- 92 acute- or early-HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy.
- This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail.These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintained in Env.

HXB2 Location gp160 (169–189)
Author Location gp120 (141–160 W6.ID)
Epitope VQKEYALFYNLDVVPIDDDNA
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21
Species (MHC) human
References Jones *et al.* 1999

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated.
- The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide ——F–K–II—N-TT vqkeyaFfyKldIIpidNdTT.
- Two T-cell lines react specifically with this peptide.

HXB2 Location gp160 (172–191)
Author Location gp120 (172–191 IIIB)
Epitope EYAFFYKLDIIPIDNDTTSY
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* Env
Species (MHC) macaque
References Lekutis *et al.* 1997

- HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkey.

HXB2 Location gp160 (172–191)
Author Location gp120 (172–191 IIIB)
Epitope EYAFFYKLDIIPIDNDTTSY?
Epitope name C5
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.

- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops.
- 4/15 responders recognized this immunodominant peptide, average SI = 7.4.

HXB2 Location gp160 (175–189)
Author Location Env (UG92005)
Epitope LFYKLDVVQIDNSTN
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V2 region of UG92005 (UG, clade D) and the Vβ usage of the TCR was not determined.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (186–208)
Author Location Env
Epitope NDNTSYRLISCNTSVITQACPKV
Epitope name HIV_env_DRB0101_3
Subtype M
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type T-cell Elispot
Keywords computational epitope prediction
References De Groot *et al.* 2004

- Bioinformatic tools (EpiMatrix and Conservatrix) were employed to predict 9 highly conserved and promiscuous class II restricted T helper epitopes from HIV-1 env sequences for a cross-clade polyepitope vaccine. 10/34 HIV-1 infected patients induced Th1 immune responses to 8/9 study peptides.
- 5/34 subjects tested responded to this peptide.
- Class II peptides containing putative epitopes were selected to favor DRB0101 presentation, as there is a transgenic mouse model for this allele for future vaccine studies. The highest scoring DRB0101 sequence of this peptide was YRLISCNTS.

HXB2 Location gp160 (186–215)
Author Location gp120 (191–220 NL43)
Epitope NDTTSYTLTSCNTSVITQACPKVSFEPIPI
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* gp120, gp160
Species (MHC) human
References Sitz *et al.* 1999

- There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients.
- Over 30% of vaccinees had a stimulation index of greater than 5 to this peptide.

HXB2 Location gp160 (188–207)
Author Location gp120 (89.6)
Epitope NTKYRLISCNTSVITQACPK
Epitope name Peptide 17
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in only 1/10 BALB/c mice tested, but was one of the most reactive in CBA/J mice, reacting with 9/10 mice.

HXB2 Location gp160 (188–207)
Author Location gp120 (190–209 89.6)
Epitope NTKYRLISCNTSVITQACPK
Immunogen Vaccine

Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse (H-2^k)
Keywords immunodominance
References Dai *et al.* 2001

- Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence.
- This peptide was recognized by 9/10 CBA/J with an average SI of 9.8, one of the two immunodominant peptides in CBA/J mice, and not by BALB/c mice, so is considered to be uniquely immunodominant for H-2^k
- Uniquely immunodominant sequences tended to be in the inner domain of the protein.

HXB2 Location gp160 (190–212)
Author Location Env (185–215)
Epitope SYRLISCNTSVITQACPKVSFEP
Epitope name HIV_env_DRB0101_62
Subtype M
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type T-cell Elispot
Keywords computational epitope prediction
References De Groot *et al.* 2004

- Bioinformatic tools (EpiMatrix and Conservatrix) were employed to predict 9 highly conserved and promiscuous class II restricted T helper epitopes from HIV-1 env sequences for a cross-clade polyepitope vaccine. 10/34 HIV-1 infected patients induced Th1 immune responses to 8/9 study peptides.
- 1/34 subjects tested responded to this peptide.
- Class II peptides containing putative epitopes were selected to favor DRB0101 presentation, as there is a transgenic mouse model for this allele for future vaccine studies.The highest scoring DR B0101 sequence of this peptide was NTSVITQA.

HXB2 Location gp160 (192–211)
Author Location gp120 (192–211 IIIB)
Epitope KLTSCNTSVITQACPKVSFE?
Epitope name D2
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 3.6.

HXB2 Location gp160 (193–218)
Author Location gp120 (193–218)
Epitope LTSCNSVITQACPKVSFEPIPIHYC
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (MHC) mouse (H-$2^{d,\ b}$)
References Sjolander *et al.* 1996

- Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein.

HXB2 Location gp160 (198–212)
Author Location Env (1007)
Epitope TSVITQACPKVSFEP
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCRs for two clonotypes was Vβ3 and Vβ8.1-2.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (198–215)
Author Location Env (1007)
Epitope TSVITQACPKVSFEPIPI
Immunogen Vaccine

Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was Vβ6.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (199–211)
Author Location Env (204–216)
Epitope SVITQACSKVSFE
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) macaque
References Nehete *et al.* 1993

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice.
- A weak or transient proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys.

HXB2 Location gp160 (199–211)
Author Location Env (204–216)
Epitope SVITQACSKVSFE
Immunogen HIV-1 infection
Species (MHC) human, chimpanzee
References Nehete *et al.* 1998b

- HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env.

HXB2 Location gp160 (199–211)
Author Location gp120 (204–216)
Epitope SVITQACSKVSFE
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-$2^{bxk, sxd}$)
References Sastry & Arlinghaus 1991

- Peptides induced T-cell proliferative response in mice representing four haplotypes.

HXB2 Location gp160 (200–214)
Author Location gp120 (205–219 LAI)
Epitope VITQACPKVSFEPIP
Subtype B
Immunogen Peptide-HLA interaction
Species (MHC) human (HLA-DR)
Keywords binding affinity
References Gaudebout *et al.* 1997

- Peptide binds to both HLA-DR*1101 and HLA-DR*0401 with high affinity.
- Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding.

HXB2 Location gp160 (201–212)
Author Location Env (1007)
Epitope ITQACPKVSFEP
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was Vβ3.
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (TSVITQACPKVSFEP and ITQACPKVSFEPIPI)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.

- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (206–220)
Author Location Env (1007)
Epitope PKVSFEPIPIHYCAP
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing
References Surman *et al.* 2001

- This epitope is located in the C2 region of 1007 (US, clade B) and 12 hybridomas recognized the peptide with Vβ usage of Vβ4,6,7,8.1-2,8.3,11,12 and others not determined.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (206–220)
Author Location Env (gp160)
Epitope PKVSFEPIPIHYCAP
Subtype B, D
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* Env *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H2b)
Assay type cytokine production, CD4 T-cell Elispot - IFNγ
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization, vaccine antigen design
References Zhan *et al.* 2004

- To develop a polyvalent Env vaccine, subtype specific B and D T-helper epitopes were identified, and mixtures of strain 1007, clade B, or UG92005, clade D envelopes were given to C57BL/6J mice. Mice were intramuscularly immunized with recombinant DNA, then intraperitoneally with rVV and finally with env protein in CFA. A dilution of 1/100 could still elicit type specific responses, and responses persisted with different prime boost combinations.
- Priming with 1007 and UG92005 env's induced both Env-specific (SNNTVGNPIILPCRI and AMYAPPIAGLIQCSS) and cross-reactive (PKVSFEPIPIHYCAP, C2, GNIRQAHCN-VSKAKW, V3-C3) Th responses in murine spleen cells.

HXB2 Location gp160 (206–225)
Author Location gp120 (211–230 MN)
Epitope PKISFEPIPIHYCAPAGFAI
Epitope name 1957
Subtype B
Immunogen Vaccine
Vector/Type: DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) guinea pig
Keywords vaccine-specific epitope characteristics, Th1
References Chattergoon *et al.* 2002

- Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.
- A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.
- 5/5 animals vaccinated with rec gp120 responded by DTH to this peptide, as did 2/6 vaccinated with plasmid gp120 DNA.

HXB2 Location gp160 (206–230)
Author Location gp120 (206–230)
Epitope PKVSFEPIPIHYCAPAGFAILKCNN
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (MHC) mouse (H-$2^{d,\ b}$)
References Sjolander *et al.* 1996

- Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein.

HXB2 Location gp160 (208–218)
Author Location Env (UG92005)
Epitope ITFEPIPIHYC
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing
References Surman *et al.* 2001

- This epitope is located in the C2 region of UG92005 (UG, clade D) and its was recognized by two hybridomas with Vβ usage Vβ12 and not determined.
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (PKITFEPIPIHYCAP and ITFEPIPIHYCAPAG)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (208–222)
Author Location Env (UG92005)
Epitope ITFEPIPIHYCAPAG
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the C2 region of UG92005 (UG, clade D) and it was recognized by five hybridomas with Vβ usage Vβ5, 8.2, 12 and not determined.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (208–227)
Author Location gp120 (210–229 89.6)
Epitope VSFQPIPIHYCVPAGFAMLK
Epitope name Peptide 19
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in 6/10 BALB/c mice tested, and in 6/10 CBA/J mice.

HXB2 Location gp160 (209–220)
Author Location gp120 (MN)
Epitope SFEPIPIHYCAP
Epitope name SP12
Subtype B

Immunogen HIV-1 infection
Species (MHC) human (DR)
Assay type cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords HAART, ART, vaccine-specific epitope characteristics, acute infection, cross-presentation by different HLA
References Malhotra *et al.* 2003

- 92 acute- or early-HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymphoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy.
- This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail. The CD4+ clones showed MHC-restricted cytotoxicity and secreted high levels of cytokines when stimulated. These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintained in Env.
- Seven out of 12 clones recognized this conserved C3 region of gp120. Clone one was mapped to the optimal epitope and was found to be presented by HLA-DR. The peptide showed promiscuous binding to DRB1*0101, DRB1*0401, DRB1*1302, DRB1*0701, DRB1*0901, DRB4*0101, DRB5*0101.

HXB2 Location gp160 (210–218)
Author Location Env (186–194 1035)
Epitope FEPIPIHYC
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia prime with gp120 boost *Strain:* B clade 1035 *HIV component:* Env *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (Class II I Ab)
Assay type proliferation, T-cell Elispot
Keywords epitope processing, vaccine-induced epitopes, escape, TCR usage
References Zhan *et al.* 2003

- A very narrow Th response was stimulated in C57BL/6 mice vaccinated with vaccinia expressed HIV-1 env clone 1035. Five of seven different Th hybridomas isolated from five immunized mice immunized reacted with the peptide PKVSFEPIPIHYCAP, located in the C2 region of gp120. TCR Vβ usage indicated each of the clones was unique. Splenic populations from other C57BL/6 mice immunized with 1035 env confirmed that the gp120 specific T-helper response was focused on the PKVSFEPIPIHYCAP peptide. The authors suggest the protein structural context may contribute to the immunodominance of this peptide.
- The minimal epitope was mapped for one of the hybridomas, and was FEPIPIHYC.
- The natural variant, fDpipihyc, did not stimulate a response in three of the hybridomas.

HXB2 Location gp160 (210–223)
Author Location gp120 (215–228)
Epitope FEPIPIHYCAFPGF
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-2^{bxk})
References Sastry & Arlinghaus 1991

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160.

HXB2 Location gp160 (212–231)
Author Location gp120 (221–240 W6.ID)
Epitope PIPIHYCAPAGFAILKCNNK
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21
Species (MHC) human
References Jones *et al.* 1999

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated.
- Two T-cell lines react specifically with this peptide.

HXB2 Location gp160 (212–231)
Author Location gp120 (212–231 IIIB)
Epitope PIPIHYCAPAGFAILKCNNK?
Epitope name D4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 3/15 responders recognized this peptide, average SI = 4.2.

HXB2 Location gp160 (214–220)
Author Location Env (1007)
Epitope PIHYCAP
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^{b})
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was not determined.

- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (PKVSFEPIPIHYCAP and PIHYCAPAGFAILKC)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (215–225)
Author Location Env (1007)
Epitope IHYCAPAGFAI
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was not determined.
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (EPIPIHYCAPAGFAI and IHYCAPAGFAILKCN)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (216–225)
Author Location Env (UG92005)
Epitope HYCAPAGFAI
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the C2 region of UG92005 (UG, clade D) and Vβ usage of its TCR was not determined.
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (EPIPIHYCAPAGFAI and HYCAPAGFAILKCND)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).

- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (220–234)
Author Location gp120 (225–240 SF2)
Epitope PAGFAILKCNNKTFN
Immunogen in vitro stimulation or selection
Species (MHC)
References Manca *et al.* 1993
- T-cell line derived from unprimed, uninfected individual.
- Responds to APC pulsed with either synthetic peptide or gp120.
- Human MAbs 448-D and 450-D enhance APC gp120 uptake and presentation.

HXB2 Location gp160 (220–234)
Author Location gp120 (IIIB)
Epitope PAGFAILKCNNKTFN
Epitope name pep24
Immunogen Vaccine
Vector/Type: Streptococcus gordonii *HIV component:* gp120
Species (MHC) human
Keywords immunodominance
References Pozzi *et al.* 1994
- This previously described immunodominant Th cell epitope was fused to the streptococcal surface protein M6 (emm-6.1), for expression on the surface of the bacterium Streptococcus gordonii.
- Recombinant bacteria showed efficient MHC class II mediated presentation of gp120 to T-cells by stimulation of a proliferative response in a human T cell clone specific for pep24.

HXB2 Location gp160 (220–235)
Author Location gp120 (IIIB)
Epitope PAGFAILKCNNKTFNY
Immunogen in vitro stimulation or selection
Species (MHC) human (DR2)
References Manca *et al.* 1995b
- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.
- gp120 priming induced T-cells that recognize this peptide.

HXB2 Location gp160 (220–235)
Author Location gp120 (220–235 HXB2)
Epitope PAGFAILKCNNKTFNY
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DR2)
Keywords escape
References Guzman *et al.* 1998
- Listeria monocytogenes, an intracellular pathogen which is ingested by macrophages and can escape from the phagosome to replicate in the cytoplasm, was used successfully as carrier to deliver this gp120 epitope to CD4+ T-cells.

HXB2 Location gp160 (220–235)
Author Location gp120 (191–205 HXB2)
Epitope PAGFAILKCNNKTFNY
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DR2)
References Fenoglio *et al.* 1999
- gp120 pep24 epitope exhibited antagonistic activity against proliferation of gp120-specific T-cells when flanked by unrelated amino acid sequence.
- The glutathione S-transferase (GST)-peptide system can be used to display peptides; antigenicity was maintained when this peptide was expressed at the C-term end, but antagonism resulted when this peptide was expressed at the N-term end.

HXB2 Location gp160 (222–241)
Author Location gp120 (222–241 IIIB)
Epitope GFAILKCNNKTFNGTGPCTN?
Epitope name D5
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994
- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 2/15 responders recognized this peptide, average SI = 4.8.

HXB2 Location gp160 (223–231)
Author Location gp120 (238–246 HXB2)
Epitope FAILKCNNK
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human
Keywords TCR usage
References Li Pira *et al.* 1998
- Clonal heterogeneity was broad for a recall response to tetanus toxoid or PPD, but oligoclonal to primary HIV antigens, dominated in this case by TCR Vβ 22 usage.
- Donor of PBMC that recognized this epitope had HLA-DR alleles 2 and 6.
- The only (detected) immunogenic variant of this epitope was derived from strain NOF (YAILKCNNK)

HXB2 Location gp160 (223–231)
Author Location gp120 (194–202 HXB2)
Epitope FAILKCNNK
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DR2, 6)
References Manca *et al.* 1996
- Epitope was the minimal stimulatory sequence defined for two Th lines stimulated *in vitro*.

- One Th line was stimulated by gp120, one by a Glutathione-S-transferase (GST)-peptide fusion.
- Alanine substitutions at position 914, 196, and 202 abrogated activity for the GST-peptide stimulated line, but not for a gp120 stimulated line.
- Constructs combining GST and the PAGFAILKCNNKTFNY gp120 peptide at the C-term end of GST stimulated Th cells but not at the N-term end.

HXB2 Location gp160 (223–231)
Author Location gp120 (194–202 HXB2)
Epitope FAILKCNNK
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DR2, 6)
References Manca *et al.* 1996

- Epitope was the minimal stimulatory sequence defined for two Th lines stimulated *in vitro*.
- One Th line was stimulated by p66, one by a Glutathione-S-transferase (GST)-peptide fusion protein.
- Alanine substitutions at position 914, 196, and 202 abrogated activity for the GST-peptide stimulated line, but not for a gp120 stimulated line.
- Constructs linking GST to the PAGFAILKCNNKTFNY gp120 peptide at the C-term end of GST stimulated Th cells, constructs linking at the N-term end did not.
- The C and N termini of GST are not intrinsically permissive or non-permissive, presentation is epitope specific (see SSTVNDIQKLV for contrast)

HXB2 Location gp160 (223–231)
Author Location gp120 (237–245 SF2, HXB2)
Epitope FAILKCNNK
Immunogen
Species (MHC) mouse (H-2^d)
Keywords inter-clade comparisons, immunodominance
References Fenoglio *et al.* 2000

- This peptide is an immunodominant Th epitope in BALB/c mice.
- Substitutions in positions 237, 241, 243, 244 with Ala all cause reduced recognition.
- Most natural analogs they tested did not cross-react, including peptides based on clade A, B, C, D, E and O sequences.
- Position 237 and 244 when substituted with Ala cause an antagonistic response and the natural analogues of this epitope to loose antigenicity.
- Some of the naturally occurring variants also cause an antagonistic response.

HXB2 Location gp160 (230–245)
Author Location gp120 (IIIB)
Epitope NKTFNGKGPCTNVSTY
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (232–251)
Author Location gp120 (232–251 IIIB)
Epitope TFNGTGPCTNVSTVQCTHGI?
Epitope name E1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 3/15 responders recognized this peptide, average SI = 3.9.

HXB2 Location gp160 (235–247)
Author Location gp120 (240–252)
Epitope GTGPCTNVSTVQC
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) macaque
References Nehete *et al.* 1993

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice.
- Proliferative response to this peptide was observed in 1/3 immunized rhesus monkeys, with a weak transient response in the other two.

HXB2 Location gp160 (238–257)
Author Location gp120 (240–249 89.6)
Epitope PCTNVSTVQCTHGIRPVVST
Epitope name Peptide 22
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was highly reactive in 6/10 BALB/c mice tested, but not in any (0/10) CBA/J mice.

HXB2 Location gp160 (240–255)
Author Location gp120 (IIIB)
Epitope TNVSTVQCTHGRPIY
Immunogen in vitro stimulation or selection

Species (MHC) human
References Manca *et al.* 1995b
- Peptide stimulation of PBMC from non-infected individuals *in vitro*.

HXB2 Location gp160 (242–261)
Author Location gp120 (242–261 IIIB)
Epitope VSTVQCTHGIRPVVSTQLLL?
Epitope name E2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994
- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 3.4.

HXB2 Location gp160 (242–261)
Author Location gp120 (242–261 IIIB)
Epitope VSTVQCTHGIRPVVSTQLLL
Immunogen SHIV infection
Species (MHC) macaque (DRB1*0406)
References Lekutis & Letvin 1997
- A novel C2 region Th epitope was described in SHIV-89.6 infected Macaca mulatta.

HXB2 Location gp160 (244–266)
Author Location Env
Epitope TVQCTHGIRPVVSTQLLLNGSLA
Epitope name HIV_env_DRB0101_11
Subtype M
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type T-cell Elispot
Keywords computational epitope prediction
References De Groot *et al.* 2004
- Bioinformatic tools (EpiMatrix and Conservatrix) were employed to predict 9 highly conserved and promiscuous class II restricted T helper epitopes from HIV-1 env sequences for a cross-clade polyepitope vaccine. 10/34 HIV-1 infected patients induced Th1 immune responses to 8/9 study peptides.
- 1/34 subjects tested responded to this peptide.
- Class II peptides containing putative epitopes were selected to favor DRB0101 presentation, as there is a transgenic mouse model for this allele for future vaccine studies. The highest scoring DR B0101 sequence of this peptide was RPVVSTQL.

HXB2 Location gp160 (246–268)
Author Location Env (438–460)
Epitope QCTHGIRPVVSTQLLLNGSLAEE
Epitope name HIV_env_DRB0101_02
Subtype M
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type T-cell Elispot
Keywords computational epitope prediction
References De Groot *et al.* 2004
- Bioinformatic tools (EpiMatrix and Conservatrix) were employed to predict 9 highly conserved and promiscuous class II restricted T helper epitopes from HIV-1 env sequences for a cross-clade polyepitope vaccine. 10/34 HIV-1 infected patients induced Th1 immune responses to 8/9 study peptides.
- 1/34 subjects tested responded to this peptide.
- Class II peptides containing putative epitopes were selected to favor DRB0101 presentation, as there is a transgenic mouse model for this allele for future vaccine studies. The highest scoring DRB0101 sequence within this peptide was PVVSTQLLL.

HXB2 Location gp160 (250–265)
Author Location gp120 (IIIB)
Epitope GIRPIVSTQLLLNGSC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b
- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (252–271)
Author Location gp120 (252–271 IIIB)
Epitope RPVVSTQLLLNGSLAEEEVV?
Epitope name E3
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994
- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, average SI = 7.4.

HXB2 Location gp160 (262–281)
Author Location gp120 (262–281 IIIB)
Epitope NGSLAEEEVVIRSVNFTDNA?
Epitope name E4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 2/15 responders recognized this peptide, average SI = 3.1.

HXB2 Location gp160 (264–287)
Author Location gp120 (269–292 NL43)
Epitope SLAEEEVVIRSANFTDNAKTIIVQ
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43
HIV component: gp120, gp160
Species (MHC) human
References Sitz *et al.* 1999

- There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients.
- 50% of vaccinees had a stimulation index of greater than 5 to this peptide.

HXB2 Location gp160 (269–283)
Author Location gp120 (269–283 IIIB, B10)
Epitope EVVIRSANFTDNAKT
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (269–291)
Author Location Env
Epitope EVVIRSENFTNNAKTIIVQLNES
Epitope name HIV_env_DRB0101_7
Subtype M
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type T-cell Elispot
Keywords computational epitope prediction
References De Groot *et al.* 2004

- Bioinformatic tools (EpiMatrix and Conservatrix) were employed to predict 9 highly conserved and promiscuous class II restricted T helper epitopes from HIV-1 env sequences for a cross-clade polyepitope vaccine. 10/34 HIV-1 infected patients induced Th1 immune responses to 8/9 study peptides.
- 1/34 subjects tested responded to this peptide.
- Class II peptides containing putative epitopes were selected to favor DRB0101 presentation, as there is a transgenic mouse model for this allele for future vaccine studies. The highest scoring DRB0101 sequence of this peptide was NFTNNAKTI.

HXB2 Location gp160 (270–285)
Author Location gp120 (IIIB)
Epitope VVIRSDNFTNNAKTIC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (272–291)
Author Location gp120 (272–291 IIIB)
Epitope IRSVNFTDNAKTIIVQLNTS?
Epitope name E5
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops.
- 4/15 responders recognized this immunodominant peptide, average SI = 5.0.

HXB2 Location gp160 (274–288)
Author Location gp120 (274–288 IIIB, B10)
Epitope SANFTDNAKTIIVQL
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (274–296)
Author Location Env
Epitope SENFTNNAKIIIVQLNESVVINV
Epitope name HIV_env_DRB0101_5
Subtype M
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type T-cell Elispot
Keywords computational epitope prediction
References De Groot *et al.* 2004

- Bioinformatic tools (EpiMatrix and Conservatrix) were employed to select 9 highly conserved and promiscuous class II restricted T helper epitopes from HIV-1 env sequences for a cross-clade vaccine. 10/34 HIV-1 infected patients induced Th1 immune responses to the 9 study peptides.
- 1/26 subjects tested responded to this peptide.

- Class II peptides containing putative epitopes were selected to favor DRB0101 presentation, as there is a transgenic mouse model for this allele for future vaccine studies. The highest scoring DRB0101 sequence of this peptide was AKIIIVQLN.

HXB2 Location gp160 (276–295)
Author Location gp120 (MN)
Epitope NFTDNAKTIIVHLNESVQIN
Epitope name NN20
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords acute infection
References Malhotra *et al.* 2003

- 92 acute- or early-HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy.
- This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail.These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintained in Env.

HXB2 Location gp160 (280–296)
Author Location gp120 (IIIB)
Epitope NAKTIIVQLNESVAIC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (288–307)
Author Location gp120 (290–309 89.6)
Epitope LNESVVINCTRPNNNTRRRL
Epitope name Peptide 27
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in only 1/10 BALB/c mice tested, but reacted in 8/10 CBA/J mice.

HXB2 Location gp160 (289–297)
Author Location gp120 (292–300 SF2)
Epitope NESVAINCT
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF2 *HIV component:* gp120
Species (MHC) human
References Botarelli *et al.* 1991

- A non-glycosylated form of SF2 gp120, env 2-3, was used as an immunogen – 20% of T-cell clones do not recognize the glycosylated form.

HXB2 Location gp160 (290–306)
Author Location gp120 (296–312 LAI)
Epitope SVVEINCTRPNNNTRKS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (290–314)
Author Location Env
Epitope ESVVINCTRPNNNTRRSIHIGPG
Epitope name HIV_env_DRB0101_14
Subtype M
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type T-cell Elispot
Keywords computational epitope prediction
References De Groot *et al.* 2004

- Bioinformatic tools (EpiMatrix and Conservatrix) were employed to predict 9 highly conserved and promiscuous class II restricted T helper epitopes from HIV-1 env sequences for a cross-clade polyepitope vaccine. 10/34 HIV-1 infected patients induced Th1 immune responses to 8/9 study peptides.
- 1/34 subjects tested responded to this peptide.
- Class II peptides containing putative epitopes were selected to favor DRB0101 presentation, as there is a transgenic mouse model for this allele for future vaccine studies.The highest scoring DR B0101 sequence of this peptide was TRPNNNTRR.

HXB2 Location gp160 (292–310)
Author Location gp120 (292–310 IIIB)
Epitope VEINCTRPNNNTRKRIRIQ?
Epitope name F1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- Only 1/15 responders recognized this peptide, but it had the highest SI in the study of 9.9.

HXB2 Location gp160 (296–307)
Author Location gp120 (301–324 RF)
Epitope CTRPNNNTRKSI
Immunogen HIV-1 infection
Species (MHC)
Keywords epitope processing
References de Lorimier *et al.* 1994

- Proton NMR spectroscopy was employed to analyze the solution conformation of a hybrid peptide, T1-SP10RF, in order to better understand the immunogenicity of its' T helper (KQIINMWQEVGKAMYA, CTRPNNNTRKSI), CTL (SITKGPGRVIYATG) and B-cell epitopes (RKSITKGPGRVIYATG).
- This epitope embedded in the T1-SP10RF peptide does not form a helical amphipathic conformation. It lacks random-coil conformations, and this may make a peptide less susceptible to complete proteolytic degredation and be favored within epitopes.

HXB2 Location gp160 (296–314)
Author Location gp120 (303–321 IIIB)
Epitope CTRPNNNTRKSIRIQRGPG(Y)
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (MHC) goat
References Palker *et al.* 1989

- Goats were immunized with peptides containing V3 type-specific neutralizing determinants coupled to T1.

HXB2 Location gp160 (297–321)
Author Location gp120 (302–324 MN)
Epitope TRPNYNKRKRIHIGPGRAFYTTK
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN *HIV component:* V3
Species (MHC) mouse (H-2^{d})
References Oscherwitz *et al.* 1999b

- Epitope presented as a tandem repeat (eight copies) elicits stronger B-cell and T-cell responses than the epitope presented as a single copy.
- This study indicates that the increased response was not due to neodeterminants created at the junction of the peptides, but rather due to an epitope density effect, increased immunogenicity through a high ratio of epitope to protein.

HXB2 Location gp160 (297–330)
Author Location Env (303–335 BX08)
Epitope TRPNNNTRKSIHIGPGRAFYATGEIIGDIRQAH
Immunogen Vaccine
Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 6/10 reacted to this peptide.
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in five vaccinees.
- None of the 12 tested had an IgG response to gp120 or gp160 and vaccinees could be differentiated from HIV-1 seropositive individuals with a commercial HIV detection kit – no neutralizing antibodies were observed.

HXB2 Location gp160 (298–307)
Author Location Env (UG92005)
Epitope RPYNNTRKGI
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^{b})
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by a hybridoma with Vβ usage not determined.
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (TINCTRPYNNTRKGI and RPYNNTRKGIHIGPG)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^{b} transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^{b} restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).

- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (298–319)
Author Location gp120 (300–319 89.6)
Epitope RPNNNTRRRLSIGPGRAFYA
Epitope name Peptide 28
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in 7/10 BALB/c mice tested, and in 5/10 CBA/J mice.

HXB2 Location gp160 (301–325)
Author Location gp120 (IIIB)
Epitope NNTRKSIRIQRGPGRAFVTIGKIGN
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* Env, Rev *Adjuvant:* QS21
Species (MHC) mouse
Keywords Th1
References Sasaki *et al.* 1998

- The env response is what is being sought, but co-expression of rev is required.
- Intramuscular versus nasal vaccination with DNA vaccine with a QS-21 adjuvant was studied.
- QS-21 enhanced the IgG2a response mediated via Th1 cytokines IFNγ and IL-2 and delayed type hypersensitivity (DTH) in response to the V3 peptide was measured by a foot pad swelling test Sasaki *et al.* [1998]

HXB2 Location gp160 (302–315)
Author Location gp120 (307–322 IIIB)
Epitope NTRKSIRIQRGPGR
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* V3
Species (MHC) mouse
References Goodman-Snitkoff *et al.* 1990

- Identification of putative Th epitopes that can stimulate an antibody response in peptide-immunized mice.

HXB2 Location gp160 (302–321)
Author Location gp120 (302–321 IIIB)
Epitope NTRKRIRIQRGPGRAFVTIG?
Epitope name F2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 5.6.

HXB2 Location gp160 (302–327)
Author Location gp120 (307–332 MN)
Epitope NKRKRIHIGPGRAFYTTKNIIGTIR
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN *HIV component:* V3 *Adjuvant:* Montanide (ISA 51)
Species (MHC) mouse
References Anderson *et al.* 2001

- Hypervariable epitope constructs (HECs) are degenerative peptide cocktails that are made in a single peptide synthesis reaction. Vaccination with a V3 degenerative peptide cocktail containing 64 distinct peptides, NTRK-[SR]-I-[HR]-IGPG-[RQ]-AFY-[AT]-TG-[DE]-IG-[DN]-IRQ, elicited broader and more durable Th responses than the MN V3 peptide alone in BALB/c mice immunized and boosted with V3 peptides, although the MN peptide elicited a transient MN-specific V3 response.

HXB2 Location gp160 (305–321)
Author Location gp120 (312–329)
Epitope (CG)KSIRIQRGPGRAFVTIG
Immunogen HIV-1 infection
Species (MHC) human
References Adams *et al.* 1997

- Used as positive control in study examining T-cell response to four p24 Gag peptides.

HXB2 Location gp160 (308–319)
Author Location gp120 (subtype C)
Epitope (CKR)KIHIGPGQAFYT
Subtype C
Immunogen HIV-1 infection
Species (MHC) mouse (H-$2^{b,\,d,\,k,\,s}$)
Keywords Th1
References Ahluwalia *et al.* 1997

- A V3 loop peptide modified to resemble an Indian form (GPGQ) was incorporated into ISCOMS (immune stimulating complexes) or liposomes, and used to immunize mice – the IgG2a/IgG2b Ab response was enhanced by the presentation in the ISCOM suggestive of a Th1 response.

HXB2 Location gp160 (308–321)
Author Location gp120 (MN)
Epitope RIHIGPGRAFYTTK
Epitope name SP10
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN
HIV component: V3
Species (MHC) mouse (H-2^d)
References Klinman *et al.* 1995

- Hybrid T1-V3 peptide activates IL-4 and IL-6 in a dose dependent manner.
- 10-mer from V3 contributes to this response.

HXB2 Location gp160 (308–322)
Author Location gp120 (308–322 IIIB)
Epitope RIHIGPGRAFYTTKN
Immunogen
Species (MHC) human
References Furci *et al.* 1997

- 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but only 1/11 exposed-uninfected individuals recognized this peptide.
- 1/18 unexposed-uninfected controls could recognize this peptide.
- Erroneously documented as IIIB sequence - most likely MN peptide.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) macaque
References Nehete *et al.* 1993

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice.
- Despite the proliferative response to this peptide in mice and humans, no response was observed in 3 rhesus monkeys.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen HIV-1 infection
Species (MHC) human
Keywords responses in children, Th1, Th2
References Wasik *et al.* 1997

- The breadth and intensity of the CTL response and the type of Th response was studied in seven rapidly progressing HIV-1 + infants.
- IL-2 and γ IFN production from Th1 cells correlated with the CTLp frequency against HIV-1 Gag, Env, Nef and Pol.
- IL-4 production from Th2 cells was inversely correlated with the CTLp frequency.
- The HIV-1 + children with strong CTL responses had levels of anti-CD3 MAb induction of Th1 cells comparable to uninfected children.
- The children that did not mount a good CTL response had dramatically decreased numbers of Th1 relative to Th2 cells.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen HIV-1 infection
Species (MHC) human
Keywords responses in children, kinetics, Th1
References Wasik *et al.* 2000

- Th responses measured by IL-2 responses to P18 and T1 in HIV-1 infected infants were undetectable at less than 1 month of age, and remained low in children with AIDS symptoms, but increased with age in children with slowly progressive disease.
- The kinetics and intensity of the CTL activity during the first year of life was related to the child's ability to make Th1 responses.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen
Species (MHC) human
References Pinto *et al.* 1995

- CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 MN)
Epitope RIHIGPGRAFYTTKN
Epitope name P18
Immunogen
Species (MHC) human
References Pinto *et al.* 1995

- CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1989

- IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1991a

- Peptides stimulate Th cell function and CTL activity in similar patient populations.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18

Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) human
References Clerici *et al.* 1991b

- Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen
Species (MHC) human
References Clerici *et al.* 1992

- Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1997

- used in a study of the influence of pentoxifylline on HIV specific T-cells.

HXB2 Location gp160 (308–322)
Author Location gp120 (MN)
Epitope RIHIGPGRAFYTTKN
Immunogen
Species (MHC) human
References Clerici *et al.* 1992

- Epitope P18 MN: Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men.

HXB2 Location gp160 (308–322)
Author Location gp160 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human
Keywords immunodominance
References Wasik *et al.* 1999

- IL-2 responses associated with beta-chemokine expression were detectable at birth in the majority of uninfected infants born to HIV+ mothers, declining by age 6 months.
- In both uninfected and infected infants of HIV-positive mothers, responses to the T1 peptide (KQIINMWQEVGKAMYA) were more frequent than responses to P18.
- T1 is a highly conserved epitope, whereas P18 has a higher mutation rate due to its location in the immunodominant V3 loop region.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen HIV-1 infection
Species (MHC) human
References Kaul *et al.* 1999

- Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases)
- Helper epitopes used in this study were noted to be previously described Clerici *et al.* [1989], and were not explicitly described in Kaul *et al.* [1999]

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human
Keywords inter-clade comparisons, responses in children, mother-to-infant transmission
References Kuhn *et al.* 2001a

- In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4.
- The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents.
- 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breastfeeding.
- Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 MN)
Epitope RIHIGPGRAFYTTKN
Epitope name P18
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human
Keywords inter-clade comparisons, responses in children, mother-to-infant transmission
References Kuhn *et al.* 2001a

- In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4.
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- 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding.
- Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.

HXB2 Location gp160 (308–322)
Author Location Env (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18IIIB
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
Keywords mother-to-infant transmission
References Clerici *et al.* 1993a

- Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected.
- PBL from 10/21 of the mother showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.

HXB2 Location gp160 (308–322)
Author Location Env (MN)
Epitope RIHIGPGRAFYTTKN
Epitope name P18MN
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
Keywords mother-to-infant transmission
References Clerici *et al.* 1993a

- Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected.
- PBL from 10/21 of the mother showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.

HXB2 Location gp160 (308–322)
Author Location Env (IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18IIIB
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
References Clerici *et al.* 1994a

- Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection.
- Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.

HXB2 Location gp160 (308–322)
Author Location Env (MN)
Epitope RIHIGPGRAFYTTKN
Epitope name P18MN
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
References Clerici *et al.* 1994a

- Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection.
- Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.

HXB2 Location gp160 (308–322)
Author Location HIV-1 (IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18IIIB
Subtype B
Immunogen HIV-1 infection
Species (MHC)
Assay type cytokine production
References Clerici *et al.* 1994b

- IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.

HXB2 Location gp160 (308–322)
Author Location HIV-1 (MN)
Epitope RIHIGPGRAFYTTKN
Epitope name P18MN
Subtype B
Immunogen HIV-1 infection
Species (MHC)
Assay type cytokine production
References Clerici *et al.* 1994b

- IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.

HXB2 Location gp160 (308–322)

Author Location Env (315–329)
Epitope RIHIGPGRAFYTTKN
Epitope name P18 MN
Immunogen HIV-1 infection
Species (MHC) human
Assay type cytokine production
Keywords mother-to-infant transmission
References Kuhn *et al.* 2001b

- The proliferative responses in cord blood at delivery to a cocktail of HIV Envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery.
- The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).

HXB2 Location gp160 (308–322)
Author Location Env (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18 IIB
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type proliferation
Keywords responses in children, mother-to-infant transmission
References Kuhn *et al.* 2001b

- T helper proliferative responses in cord blood at delivery to a cocktail of HIV envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery.
- The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).

HXB2 Location gp160 (308–322)
Author Location Env (gp160) (317–331 MN)
Epitope RIHIGPGRAFYTTKN
Epitope name P18
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Country South Africa.
Assay type proliferation
Keywords responses in children, variant cross-recognition or cross-neutralization
References Meddows-Taylor *et al.* 2004

- Viral isolates (gp160) from 16 vertically HIV-1 infected children (8 T-helper cell Env responders and 8 non-responders) were analyzed for variation after comparison with Env peptide sequences (conserved regions T1, T2 and TH4.1, hypervariable regions P18 MN and P181 IIIB) used for in vitro stimulation.
- No correlation between the age, clinical category (mild or severe), HIV-1 viral load and the degree of epitope variation was established.

HXB2 Location gp160 (308–322)
Author Location Env (gp160) (317–331 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Country South Africa.
Assay type proliferation
Keywords responses in children
References Meddows-Taylor *et al.* 2004

- Viral isolates (gp160) from 16 vertically HIV-1 infected children (8 T-helper cell Env responders and 8 non-responders) were analyzed for variation after comparison with Env peptide sequences (conserved regions T1, T2 and TH4.1, hypervariable regions P18 MN and P181 IIIB) used for in vitro stimulation.
- No correlation between the age, clinical category (mild or severe), HIV-1 viral load and the degree of epitope variation was established.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen HIV-1 infection
Species (MHC) human (DR)
References Baier *et al.* 1995

- Linked HIV-1 T1 and P18 peptides to anti-HLA-DR and IgD Fab fragments to enhance uptake by antigen presenting cells thus increase immunogenicity.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) mouse (H-2 A^d)
References Takahashi *et al.* 1990

- Induces both class II restricted CD4+ Th cells, and class I restricted CD8+ CTL.

HXB2 Location gp160 (308–322)
Author Location gp120 (315–329 IIIB)
Epitope RIQRGPGRAFVTIGK
Epitope name P18
Immunogen Peptide-HLA interaction

Species (MHC) mouse (H-2 I-A^d)
References Takeshita *et al.* 1995

- Binds Class II H-2 I-A^d requiring riqrgPgRaFvti, and Class I H-2 D^d, requiring iGPgRaFvtI.

HXB2 Location gp160 (308–322)
Author Location Env (IIIB)
Epitope RIQRGPRAFVTIGK
Epitope name P18
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* MIP-1α
Species (MHC) mouse (H-2^d)
Keywords Th1
References Lu *et al.* 1999

- MIP-1a expression plasmid co-inoculated with a DNA vaccine consisting of HIV-1 pCMV160IIIB and pcREV enhanced the HIV-specific T-cell immune response as measured by a CTL test against using V3 peptide pulsed targets, and a DTH test to V3 peptide.
- The IgG1/IgG2a response was lowered with co-inoculation of MIP-1 alpha, suggesting it preferentially elicits a Th1 response.

HXB2 Location gp160 (308–327)
Author Location gp120 (306–325 MN)
Epitope RIHIGPGRAFYTTKNIIGIT
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101)
References Hayball *et al.* 1997

- Tandem repeated presentation of epitope enhances binding to class II molecule and therefore induction of T-cell proliferation.
- Tandem peptides are thought to enhance proliferation through improved recruiting of CD4 to the activation complex, which can counter-balance gp120's sequestering of CD4 and consequential inhibition of a proliferative response.

HXB2 Location gp160 (309–323)
Author Location gp120 (309–323 IIIB, B10)
Epitope EQRGPGRAFVTIGKI
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (309–325)
Author Location gp120 (314–330)
Epitope IQRGPGRAFVTIGKIGN
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Caruso *et al.* 1997

- As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71.
- The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost.
- This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24.

HXB2 Location gp160 (310–328)
Author Location gp120 (310–329 89.6)
Epitope SIGPGRAFYARRNIIGDIRQ
Epitope name Peptide 29
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in 2/10 BALB/c mice tested, and in 8/10 CBA/J mice.

HXB2 Location gp160 (311–319)
Author Location
Epitope RGPGRAFVT
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade BH10 *HIV component:* gp120 *Adjuvant:* GM-CSF
Species (MHC) mouse
References Barouch *et al.* 2002

- gp120 encoding DNA co-injected with a plasmid carrying GM-CSF gave meager CD4+ T-cell responses in BALB/c mice relative to bicistronic gp120 and GMCSF cloned into the same vector and expressed from the same promoter.
- The bicistronic gp120/GM-CSF vaccine induced an approximately 10-fold increase of CD4+ T cell proliferative responses to gp120, as well as a significant increase in IL-2, IL-4, IL-10, IFNγ and GM-CSF production, compared to immunization with the monocistronic pVIJ-gp120 with GMCSF. The enhanced proliferative responses were substantiated by CD4+ T-cell Elispot.
- Both mono and bicistronic DNA vaccines induced similar CTL responses directed against the H-2Dd restricted P18 peptide RGPRAFTVTI in murine splenocytes despite the enhanced proliferative responses.

HXB2 Location gp160 (311–320)
Author Location gp120 (IIIB)
Epitope RGPGPAFVTI
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* IL-2

Species (MHC) mouse (H-2^d)
Keywords Th1
References Xin *et al.* 1998

- Intranasal immunization with IL-2 expression plasmid in addition to DNA vaccine amplifies cellular response to antigen, probably via activation of Th type 1 (Th1) cells.

HXB2 Location gp160 (311–320)
Author Location gp120 (IIIB)
Epitope RGPGPAFVTI
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* IL-15
Species (MHC) mouse (H-2^d)
Keywords Th1
References Xin *et al.* 1999

- Intranasal immunization with IL-15 expression plasmid in addition to DNA vaccine increases DTH response and CTL activity to the antigen, and decreases the serum IgG1 to IgG2a ratio, enhancing Th type 1 (Th1) cell-mediated immunity.
- Expression of IL-2 or IL-15 can enhance Th1 response to the vaccine, but they to do not appear to elicit a synergistic response.

HXB2 Location gp160 (311–320)
Author Location gp120 (IIIB)
Epitope RGPGPAFVTI
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* CD40
Species (MHC) mouse (H-2^d)
Keywords Th1, Th2
References Ihata *et al.* 1999

- CD40L expression increases DTH, and Th1-dependent responses based on enhanced IgG2a titers, with no lowering of IgG1 titers.
- Elispot assay indicated co-injection with hCD40L resulted in greater numbers of IFNγ producing Th1cells, as well as increased IL-4 producing Th2 cells.
- Results suggest hCD40L enhance both Th1 and Th2 cells, and such a pattern of induction is unique among adjuvants, as most adjuvants increase either Th1 or Th2.

HXB2 Location gp160 (311–322)
Author Location Env (IIIB)
Epitope RGPGRAFVTIGK
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* GM-CSF
Species (MHC) mouse (H-2^d)
Keywords Th1, Th2
References Kusakabe *et al.* 2000

- The timing of delivery of the pGM-CSF expression plasmid for intramuscular DNA pCMV160IIIB/REV vaccination impacts the Th response, maximizing Th2 responses when administered 3 days prior to the DNA vaccine, and Th1 responses when administered 3 days after the DNA vaccine.

HXB2 Location gp160 (314–328)
Author Location gp120 (314–328 IIIB, B10)
Epitope GRAFVTIGKIGNMRQ
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (314–341)
Author Location gp120 (319–346 NL43)
Epitope GRAFVTIGKIGNMRQAHCNISRAKWNAT
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* gp120, gp160
Species (MHC) human
References Sitz *et al.* 1999

- There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients.
- More than 25% of vaccinees had a stimulation index of greater than 5 to this peptide.

HXB2 Location gp160 (315–328)
Author Location Env (UG92005)
Epitope RAYYTTNIVGNIRQ
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by two hybridomas with Vβ usage not determined, but one used Vα 8.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).

- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (317–331)
Author Location gp120 (324–338 IIIB)
Epitope FVTIGKIGNMRQAHC
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{k, d}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (317–331)
Author Location gp160 (324–338 IIIB)
Epitope FVTIGKIGNMRQAHC
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^d)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- B10.BR (H-$2A^k$, E^k) and B10.D2 (H-$2A^d$, E^d) mice immunized with rec gp160 showed a proliferative response to this peptide.
- FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes including FVTIGKIGNMRQAHC and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (317–336)
Author Location gp120 (321–340 MN)
Epitope YTTKNIIGTIRQAHCNSRA
Epitope name 1987
Subtype B
Immunogen Vaccine
Vector/Type: DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) guinea pig
Keywords vaccine-specific epitope characteristics, Th1
References Chattergoon *et al.* 2002

- Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.
- A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.
- 4/5 animals vaccinated with rec gp120 responded by DTH to this peptide, as did 4/6 vaccinated with plasmid gp120 DNA.

HXB2 Location gp160 (317–349)
Author Location gp160 (324–356 IIIB)
Epitope FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) human, mouse (H-2^k, H-2^d)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide.
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people.
- This cluster peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k) and B10.D2 mice (H-$2A^d$, E^d), but shorter peptides from within this region stimulated H-2^k, H-2^d, H-2^b and H-2^s responses.
- IL-2 production in response to this peptide was observed in 58% (21/36) of asymptomatic HIV-infected individuals.

HXB2 Location gp160 (319–338)
Author Location gp120 (320–339 89.6)
Epitope RRNIIGDIRQAHCNISRAKW
Epitope name Peptide 30
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was highly reactive in 7/10 BALB/c mice tested, and in 7/10 CBA/J mice and was considered one of the 3 immunodominant peptides identified that were shared in both mouse strains: RRNIIGDIRQAHCNISRAKW, NNTLQQIVIKLREKFRNKTI, GTNGTEGNDIITLQCRIKQI.

HXB2 Location gp160 (319–338)
Author Location gp120 (320–339 89.6)
Epitope RRNIIGDIRQAHCNISRAKW
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse (H-2^k, H-2^d)
Keywords immunodominance
References Dai *et al.* 2001

- Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence.
- This peptide was recognized by 7/10 CBA/J and 7/10 BALB/c mice with SI > 4, averaging 6.3 and 4.8, and is considered to be promiscuously immunodominant.
- Uniquely immunodominant sequences tended to be in the inner domain of the protein.

HXB2 Location gp160 (321–336)
Author Location gp120 (IIIB)
Epitope RIIGDIRKAHCNISRY
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (322–336)
Author Location Env (1007)
Epitope IIGDIRQAHCNISRE
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V3 region of 1007 (US, clade B) and was recognized by three hybridomas with Vβ usage Vβ 6 and not determined.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (322–336)
Author Location Env (UG92005)
Epitope IVGNIRQAHCNVSKA
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by three hybridomas with Vβ usage Vβ 6, 8.1, and not determined.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (322–336)
Author Location Env (UG92005)
Epitope IVGNIRQAHCNVSKA
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)

Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by three hybridomas with Vβ usage Vβ 6, 8.1, and not determined.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (322–341)
Author Location gp120 (322–341 IIIB)
Epitope KIGNMRQAHCNISRAKWNNT?
Epitope name F4
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 7.6.

HXB2 Location gp160 (324–336)
Author Location Env (UG92005)
Epitope GNIRQAHCNVSKA
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by two hybridoma with Vβ usage Vβ8.2 and not determined.
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (IVGNIRQAHCNVSKA and GNIRQAHCNVSKAKW)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (324–338)
Author Location Env (UG92005)
Epitope GNIRQAHCNVSKAKW
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by eleven hybridomas with Vβ usage Vβ5, 7, 8.1, 8.2, 11 and not determined – a Vβ 8.1's and

Vβ 8.2 also were shown to use Vα 8, and one of the ND used Vα 2.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (324–338)
Author Location gp120 (V3)
Epitope GNIRQAHCNVSKAKW
Subtype B, D
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* Env *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H2b)
Assay type cytokine production, CD4 T-cell Elispot - IFNγ
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization, vaccine antigen design
References Zhan *et al.* 2004
- To develop a polyvalent Env vaccine, subtype specific B and D T-helper epitopes were identified, and mixtures of strain 1007, clade B, or UG92005, clade D envelopes were given to C57BL/6J mice. Mice were intramuscularly immunized with recombinant DNA, then intraperitoneally with rVV and finally with env protein in CFA. A dilution of 1/100 could still elicit type specific responses, and responses persisted with different prime boost combinations.
- Priming with 1007 and UG92005 env's induced both Env-specific (SNNTVGNPIILPCRI and AMYAPPIAGLIQCSS) and cross-reactive (PKVSFEPIPIHYCAP, C2, GNIRQAHCN-VSKAKW, V3-C3) Th responses in murine spleen cells.

HXB2 Location gp160 (327–341)
Author Location gp120 (327–341 HXB2)
Epitope RQAHCNISRAKWNNT
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* gp120
Species (MHC) mouse ($I\text{-}A^d$)
References Warren & Thomas 1992
- Minimum epitope and MHC restriction determined for CTL clone that recognizes the N-terminal flank of the V3 loop.

HXB2 Location gp160 (327–346)
Author Location gp120 (331–350 MN)
Epitope RQAHCNISRAKWNDILRQIV
Epitope name 1988
Subtype B
Immunogen Vaccine
Vector/Type: DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) guinea pig
Keywords vaccine-specific epitope characteristics, Th1
References Chattergoon *et al.* 2002
- Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.
- A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.
- 4/5 animals vaccinated with rec gp120 responded by DTH to this peptide, and 2/6 responded that were vaccinated with plasmid gp120 DNA.

HXB2 Location gp160 (330–350)
Author Location gp120 (330–349 IIIB)
Epitope HCNISRAKWNNTLKQIASKLR?
Epitope name F5
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994
- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 3/15 responders recognized this peptide, average SI = 5.5.

HXB2 Location gp160 (331–345)
Author Location gp120 (IIIB)

Epitope CNISRAQWNNTLEQI
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (332–354)
Author Location gp120 (337–359 NL43)
Epitope NISRAKWNATLKQIASKLREQFG
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43
HIV component: gp120, gp160
Species (MHC) human
References Sitz *et al.* 1999

- There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients.
- More than 30% of vaccinees had a stimulation index of greater than 5 to this peptide.

HXB2 Location gp160 (335–349)
Author Location gp120 (342–356 IIIB)
Epitope RAKWNNTLKQICSKL
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{k,\ t4,\ i5}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (335–349)
Author Location gp160 (342–356 IIIB)
Epitope RAKWNNTLKQIDSKL
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^b, H-2^s)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- B10.BR (H-$2A^k$, E^k), B10.A(5R) (H-$2A^b$, E^b) and B10.S(9R) (H-$2A^s$, E^s) mice immunized with rec gp160 showed a proliferative response to this peptide.
- FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes including RAKWNNTLKQIDSKL and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (337–356)
Author Location gp120 (341–360 MN)
Epitope KWNDTLRQIVSKLKEQFKNK
Epitope name 1989
Subtype B
Immunogen Vaccine
Vector/Type: DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) guinea pig
Keywords vaccine-specific epitope characteristics, Th1
References Chattergoon *et al.* 2002

- Hartley guinea pig were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.
- A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.
- 3/5 animals vaccinated with rec gp120 responded by DTH to this peptide, and 2/6 responded that were vaccinated with plasmid gp120 DNA.

HXB2 Location gp160 (339–359)
Author Location gp120 (340–359 89.6)
Epitope NNTLQQIVIKLREKFRNKTI
Epitope name Peptide 32
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6
HIV component: gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in 6/10 BALB/c mice tested, and in 4/10 CBA/J mice and was considered one of the 3 immunodominant peptides identified that were shared in both mouse strains: RRNIIGDIRQAHCNISRAKW, NNTLQQIVIKLREKFRNKTI, GTNGTEGNDIITLQCRIKQI.

HXB2 Location gp160 (339–359)
Author Location gp120 (340–359 89.6)
Epitope NNTLQQIVIKLREKFRNKTI
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6
HIV component: gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse (H-2^k, H-2^d)
Keywords immunodominance
References Dai *et al.* 2001

- Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence.
- This peptide was recognized by 4/10 CBA/J and 6/10 BALB/c mice with SI > 4, averaging 4.9 and 5.5 and is considered to be promiscuously immunodominant.

- Uniquely immunodominant sequences tended to be in the inner domain of the protein.

HXB2 Location gp160 (341–356)
Author Location gp120 (IIIB)
Epitope TLEQIVKKLREQFGNC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (342–361)
Author Location gp120 (342–361 IIIB)
Epitope LKQIASKLREQFGNNKTIIF?
Epitope name G1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 2/15 responders recognized this peptide, average SI = 6.0.

HXB2 Location gp160 (344–357)
Author Location gp120 (346–359)
Epitope QIVKKLREQFGNNK
Immunogen HIV-1 infection
Species (MHC) human
References Krowka *et al.* 1990

- Conjugation of HIV peptides to liposomes and rIL-2 stimulation may enhance cell-mediated responses.

HXB2 Location gp160 (349–368)
Author Location gp120 (350–369 89.6)
Epitope LREKFRNKTIAFNQSSGGD
Epitope name Peptide 33
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in 3/10 BALB/c mice tested, and in 5/10 CBA/J mice.

HXB2 Location gp160 (350–370)
Author Location gp120 (350–370 IIIB)
Epitope REQFGNNKTIIFKQSSGGDPE?
Epitope name G2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, average SI = 3.2.

HXB2 Location gp160 (353–360)
Author Location gp120 (355–362 IIIB)
Epitope FGNNKTII
Immunogen SHIV infection
Species (MHC) macaque
References Lekutis & Letvin 1997

- C3 region minimal epitope determined through fine epitope mapping.
- Cell line was lost prior to confirmation of MHC requirements.

HXB2 Location gp160 (363–372)
Author Location gp120 (368–377 LAI)
Epitope QSSGGDPEIV
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (364–378)
Author Location gp120 (364–378 IIIB, B10)
Epitope SSGGKPEIVTHSFNC
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (369–383)

Author Location gp120 (369–383 IIIB, B10)
Epitope PEIVTHSFNCGGEFF
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (380–393)
Author Location gp120 (380–393 IIIB)
Epitope GEFFYCNSTQLFNS?
Epitope name G4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords immunodominance
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops.
- 4/15 responders recognized this immunodominant peptide, average SI = 4.4.

HXB2 Location gp160 (381–395)
Author Location gp120 (IIIB)
Epitope EFFYCNTTQLFNNTW
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (391–405)
Author Location gp120 (IIIB)
Epitope FNNTWRLNHTEGTKGC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (392–411)
Author Location gp120 (392–411 IIIB)
Epitope NSTWFNSTWSTEGSNNTEGS?
Epitope name G5
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 9.3.

HXB2 Location gp160 (394–408)
Author Location gp120 (394–408 IIIB, B10)
Epitope TWFNSTWSTKGSNNT
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (399–413)
Author Location gp120 (399–413 IIIB, B10)
Epitope TWSTKGSNNTEGSDT
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (404–423)
Author Location gp120 (400–419 89.6)
Epitope GTNGTEGNDIITLQCRIKQI
Epitope name Peptide 38
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in 8/10 BALB/c mice tested, and in 6/10 CBA/J mice, and was considered one of the 3 immunodominant peptides identified that were shared in both mouse strains: RRNIIGDIRQAHCNISRAKW, NNTLQQIVIKLREKFRNKTI, GTNGTEGNDIITLQCRIKQI.

HXB2 Location gp160 (404–423)

Author Location gp120 (400–419 89.6)
Epitope GTNGTEGNDIITLQCRIKQI
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse (H-2^k, H-2^d)
Keywords immunodominance
References Dai *et al.* 2001

- Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence.
- This peptide was recognized by 4/10 CBA/J and 6/10 BALB/c mice with SI > 4, averaging 4.9 and 5.5 and is considered to be promiscuously immunodominant.
- Uniquely immunodominant sequences tended to be in the inner domain of the protein.

HXB2 Location gp160 (405–420)
Author Location Env (1007)
Epitope SNNTVGNPIILPCRI
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the V4C4 region of 1007 (US, clade B) and was recognized by 13 hybridomas with Vβ usage Vβ 4, 7, 8.1, 8.2, 10, 12 and not determined – one of the Vβ 8.2 was shown to utilize Vα 2.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (405–420)
Author Location Env (gp160) (1007)
Epitope SNNTVGNPIILPCRI
Subtype B
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* Env *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H2b)
Assay type cytokine production, CD4 T-cell Elispot - IFNγ
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization, vaccine antigen design
References Zhan *et al.* 2004

- To develop a polyvalent Env vaccine, subtype specific B and D T-helper epitopes were identified, and mixtures of strain 1007, clade B, or UG92005, clade D envelopes were given to C57BL/6J mice. Mice were intramuscularly immunized with recombinant DNA, then intraperitoneally with rVV and finally with env protein in CFA. A dilution of 1/100 could still elicit type specific responses, and responses persisted with different prime boost combinations.
- T-cell hybridoma 1007P3-23 was isolated from mice immunized with 1007, and it recognized the peptide SNNTVGNPIILPCRI of the V4/C4 region. The minimal, core peptide recognized by 10007P3-23 was NPIIL, a sequence not found in UG92005, which has a deletion in the core, so that the equivalent region in the D isolate is NNET—ITLQCRI
- Priming mixtures of 1007 and UG92005 induced both Env-specific (SNNTVGNPIILPCRI and AMYAPPIAGLIQCSS) and cross-reactive (PKVSFEPIPIHYCAP, C2, GNIRQAHCNVSKAKW, V3-C3) Th responses in murine spleen cells.

HXB2 Location gp160 (410–429)
Author Location gp120 (410–429 PV22)
Epitope GSDTITLPCRIKQFINMWQE
Immunogen HIV-1 infection
Species (MHC) human (DR4)
References Callahan *et al.* 1990

- Synthetic peptides representing natural variants were used to test for recognition in the context DR4.

HXB2 Location gp160 (410–429)
Author Location gp120 (410–429 PV22)
Epitope GSDTITLPCRIKQFINMWQE
Immunogen HIV-1 infection
Species (MHC) human (DR4(Dw10))
References Polydefkis *et al.* 1990

- Human CD4+ T-cell clones lyse recombinant vaccinia virus-infected cells that synthesize envelope gp160.

HXB2 Location gp160 (412–431)
Author Location gp120 (412–431 IIIB)
Epitope DTITLPCRIKQIINMWQKVG?
Epitope name H2
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 5.7.

HXB2 Location gp160 (416–431)
Author Location gp120 (IIIB)
Epitope LPCRIKQIINMWQEVY
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (418–436)
Author Location Env (417–435)
Epitope CRIKQIINMWQGVGKAMYA
Immunogen HIV-1 infection
Species (MHC) human, chimpanzee
References Nehete *et al.* 1998b

- HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env.

HXB2 Location gp160 (421–436)
Author Location gp120 (426–441 IIIB)
Epitope KQFINMWQEWGKAMYA
Immunogen
Species (MHC) human
References Furci *et al.* 1997

- Epitope T1 variant: 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but none reacted with this previously defined epitope.
- IIIB position 435 listed as W in this epitope as opposed to V in the sequence.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–433 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection
Species (MHC) human
Keywords responses in children, kinetics, Th1
References Wasik *et al.* 2000

- Th responses measured by IL-2 responses to P18 and T1 in HIV-1 infected infants were undetectable at less than 1 month of age, and remained low in children with AIDS symptoms, but increased with age in children with slowly progressive disease.
- The kinetics and intensity of the CTL activity during the first year of life was related to the child's ability to make Th1 responses.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–433 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection
Species (MHC) human
Keywords responses in children, Th1, Th2
References Wasik *et al.* 1997

- The breadth and intensity of the CTL response and the type of Th response was studied in seven rapidly progressing HIV-1 + infants.
- IL-2 and γ IFN production from Th1 cells correlated with the CTLp frequency against HIV-1 Gag, Env, Nef and Pol.
- IL-4 production from Th2 cells was inversely correlated with the CTLp frequency.
- The HIV-1 + children with strong CTL responses had levels of anti-CD3 MAb induction of Th1 cells comparable to those of uninfected children.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) human
References Berzofsky *et al.* 1988

- Proliferative response to T1 and T2 peptides in 14 immunized, uninfected humans.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (MHC) goat
References Palker *et al.* 1989

- Goats immunized with peptides containing V3 type-specific neutralizing determinants coupled to T1.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1989

- IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1991a

- Peptides stimulate Th cell function and CTL activity in similar patient populations.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) human
References Clerici *et al.* 1991b

- Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen
Species (MHC) human
References Clerici *et al.* 1992

- Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Immunogen Vaccine
Vector/Type: bacteriophage coat protein *Strain:* B clade MN *HIV component:* V3
Species (MHC) mouse
References di Marzo Veronese *et al.* 1994

- Epitope T1 was engineered into a filamentous bacteriophage coat protein, and the Th epitope stimulated Ab production to the V3 loop.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (MHC) chimpanzee
References Haynes *et al.* 1993

- Hybrid T1-V3 peptide immunogenicity reduced when the fusogenic domain of gp41 was added.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1997

- Used in a study of the influence of pentoxifylline on HIV specific T-cells.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen
Species (MHC) human
References Pinto *et al.* 1995

- CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers.

HXB2 Location gp160 (421–436)
Author Location gp160 (428–433 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human
Keywords immunodominance
References Wasik *et al.* 1999

- IL-2 responses associated with beta-chemokine expression were detectable at birth in the majority of uninfected infants born to HIV+ mothers, declining by age 6 months.
- T1 peptide: In both uninfected and infected infants of HIV-positive mothers, responses to the T1 peptide were more frequent than responses to P18 (RIQRGPGRAFVTIGK)
- T1 is a highly conserved epitope, whereas P18 has a higher mutation rate due to its location in the immunodominant V3 loop region.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection
Species (MHC) human
References Kaul *et al.* 1999

- Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases)
- Helper epitopes used in this study were noted to be previously described Clerici *et al.* [1989], and were not explicitly described in Kaul *et al.* [1999]

HXB2 Location gp160 (421–436)
Author Location gp120 (MN)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *Strain:* B clade MN
Species (MHC) human
References Bartlett *et al.* 1998

- C4-V3 PV (polyvalent HIV envelope synthetic peptide immunogen) consisted of T1 helper epitope presented in tandem with a V3 loop CTL epitope from one of four different North American strains.

- This was a pilot phase I study involving vaccination of ten HIV-infected subjects who were HLA-B7-positive.
- Enhanced lymphoproliferative response to peptide was observed in 5/8 vaccinees – increase in neutralizing antibody responses in 4/8 vacinees.

HXB2 Location gp160 (421–436)
Author Location gp120
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human
Keywords inter-clade comparisons, responses in children, mother-to-infant transmission
References Kuhn *et al.* 2001a

- In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4.
- The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents.
- 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breastfeeding.
- Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 RF)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection
Species (MHC)
Keywords epitope processing
References de Lorimier *et al.* 1994

- Proton NMR spectroscopy was employed to analyze the solution conformation of a hybrid peptide, T1-SP10RF, in order to better understand the immunogenicity of its' T helper (KQIINMWQEVGKAMYA, CTRPNNNTRKSI), CTL (SITKGPGRVIYATG) and B-cell epitopes (RKSITKGPGRVIYATG).
- As a free peptide, the T1 segment, a T-helper epitope is in an extended conformation with nascent helical conformation. It may form a beta strand in native gp120, and a nonnative conformation may account for the inability of free T1 peptide to elicit antibody responses, in contrast to the T1 segment in native gp120. It lacks random-coil conformations, and it is suggested that this may make the peptide less susceptible to complete proteolytic degredation, and be favored within epitopes.

HXB2 Location gp160 (421–436)
Author Location Env (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
Keywords mother-to-infant transmission
References Clerici *et al.* 1993a

- Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected.
- PBL from 10/21 of the mothers showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.

HXB2 Location gp160 (421–436)
Author Location Env (IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
References Clerici *et al.* 1994a

- Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection.
- Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.

HXB2 Location gp160 (421–436)
Author Location HIV-1 (IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Subtype B
Immunogen HIV-1 infection
Species (MHC)
Assay type cytokine production
References Clerici *et al.* 1994b

- IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.

HXB2 Location gp160 (421–436)
Author Location Env (428–443)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type proliferation

Keywords responses in children, mother-to-infant transmission
References Kuhn *et al.* 2001b

- T helper proliferative responses in cord blood at delivery to a cocktail of HIV envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery.
- The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).

HXB2 Location gp160 (421–436)
Author Location Env (gp160) (421–436)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Country South Africa.
Assay type proliferation
Keywords responses in children, variant cross-recognition or cross-neutralization
References Meddows-Taylor *et al.* 2004

- Viral isolates (gp160) from 16 vertically HIV-1 infected children (8 T-helper cell Env responders and 8 non-responders) were analyzed for variation after comparison with Env peptide sequences (conserved regions T1, T2 and TH4.1, hypervariable regions P18 MN and P181 IIIB) used for in vitro stimulation.
- No correlation between the age, clinical category (mild or severe), HIV-1 viral load and the degree of epitope variation was established.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen HIV-1 infection
Species (MHC) human (DR)
References Baier *et al.* 1995

- Linked HIV-1 T1 and P18 peptides to anti-HLA-DR and anti-IgD Fab fragments to enhance uptake by antigen presenting cells and thus increase immunogenicity.

HXB2 Location gp160 (421–436)
Author Location Env (421–436 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen Vaccine
Vector/Type: peptide *Strain:* modified B clade IIIB *HIV component:* Env
Species (MHC) mouse (Ek)
Assay type cytokine production, Th support of CTL response
Keywords binding affinity, Th1
References Ahlers *et al.* 2001

- BALB/c and A.AL were immunized with an Env-peptide vaccine construct containing the CTL epitope P18IIIB and a T helper epitope.
- Substitution of Glu (wt) to Ala, kqiinmwqAvgkamya, caused increased affinity for MHC class II Ek. This resulted in the upregulation of CD40L in the responding Th cells, and shifted the response towards Th1. Increased Th responses stimulated DCs to produce higher levels of IL-12, and B7-1 and B7-2, thus enhance CTL responses.
- The modified epitope, T1A, elicited stronger protection against increasing doses of viral challenge with vaccinia expressing HIV-1 IIIB gp120 compared to the wildtype epitope T1.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (MHC) mouse (H-2^{d})
References Klinman *et al.* 1995

- Hybrid T1-V3 peptide activates IL-4 and IL-6 in a dose dependent manner.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB, B10)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen computer prediction
Species (MHC) mouse (H-$2^{k, d, s}$)
References Cease *et al.* 1987

- 1 of 2 functional epitopes identified using an amphipathic helix epitope prediction algorithm.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{k, d, t4}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (MHC) mouse (H-2^{k})
References Ahlers *et al.* 1997b

- first identified Th epitope in HIV.

- Alanine at position 436 (instead of E in wild-type) enhances MHC binding and antigenicity of peptide by several orders of magnitude.
- Vaccines with a CTL epitope linked to a more potent helper epitope yielded greatly enhanced CTL response relative to the wildtype helper epitope.
- T1 peptide linked to CTL epitopes in four vaccine constructs used to immunize mice: KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTIGK, KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTI, KQIINMWQAVGKAMYAPPISGQIRRIQRGPGRAFVTIGK, KQIINMWQAVGKAMYAPPISGQIRRIQRGPGRAFVTI.

HXB2 Location gp160 (421–436)
Author Location gp160 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^s, H-2^d)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- B10.BR (H-$2A^k$, E^k), B10.D2 (H-$2A^d$, E^d) and B10.S(9R) (H-$2A^s$, E^s) mice immunized with rec gp160 showed a proliferative response to this peptide.
- KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including KQIINMWQEVGKAMYA and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (421–436)
Author Location gp120 (428–443 IIIB)
Epitope KQIINMWQEVGKAMYA
Epitope name T1
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (MHC) mouse (H-2Eα Eβ ^{k})
References Boehncke *et al.* 1993

- C3H $H2^k$ mice were used for immunization in the study because H-2^k mice are particularly good T1 responders – T1 can be presented by $E\alpha E\beta^k$ but not $E\alpha E\beta^b$ – the nature of the T1 class II molecular interaction was thoroughly explored.
- Alanine substitutions across peptide did not negatively affect MHC binding or effective presentation of epitope, except at three critical residues (432N, 435Q, 439K), however substitutions with larger side chains often diminished activity – only a few amino acids were found to be critical for class II interaction and for maintaining T-cell receptor specificity.
- A gain in potency was observed when 436E was replaced with A, suggesting that substitutions in positions that interfere with binding might allow the design of a more potent vaccine.

HXB2 Location gp160 (421–444)
Author Location Env (gp160) (HIV-1 IIIB)
Epitope KQIINMWQEVGKAMYAPPISGQIR
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* Env *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72), Montanide (ISA 51)
Species (MHC) macaque
Assay type proliferation
Keywords mucosal immunity
References Belyakov *et al.* 2001

- Intrarectal vaccination with a Th and CTL peptide vaccine provided better protection against intrarectal challenge with pathogenic SHIV-Ku1 than subcutaneous administered vaccine. In some animals after the initial viremia, viral loads were diminished to undetectable levels in the blood and intestine, and CD4+ T cells were better preserved.
- The CD4 T-cell proliferative response correlated with the level of the CTL response.

HXB2 Location gp160 (421–444)
Author Location gp160 (428–451 IIIB)
Epitope KQIINMWQEVGKAMYAPPISGQIR
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) human, mouse (H-2^k, H-2^b, H-2^s, H-2^d)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide.
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people.
- This cluster peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)
- IL-2 production in response to this peptide was observed in 73% (8/11) of asymptomatic HIV-infected individuals.

HXB2 Location gp160 (421–444)
Author Location gp120 (428–451 IIIB)
Epitope KQIIMNWQEVGKAMYAPPISGQIR
Epitope name T1
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (MHC) mouse ($H2^d$)
References Shirai *et al.* 1996a

- Linked to a CTL epitope from hepatitis C virus, induced CD4+ helper cells producing IL-2.

HXB2 Location gp160 (423–440)
Author Location gp120 (428–445)
Epitope FINMWQEVGKAMYAPPIS
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Caruso *et al.* 1997

- As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71.
- The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost.

- This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24.

HXB2 Location gp160 (424–438)
Author Location gp120 (424–438 IIIB, B10)
Epitope INMWQEVGKAMYAPP
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (425–439)
Author Location gp160 (432–446 IIIB)
Epitope NMWQEVGKAMYAPPI
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^{s})
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- B10.S(9R) (H-$2A^{s}$, E^{s}) mice immunized with rec gp160 showed a proliferative response to this peptide.
- KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including NMWQEVGKAMYAPPI and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (425–439)
Author Location gp120 (432–446 IIIB)
Epitope NMWQEVGKAMYAPPI
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2^{t4})
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (426–441)
Author Location gp120 (IIIB)
Epitope MWQEVGKAMYAPPIGC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (430–444)
Author Location gp120 (437–451 IIIB)
Epitope VGKAMYAPPISGQIR
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{k,\ d,\ i5,\ t4}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (430–444)
Author Location gp160 (437–451 IIIB)
Epitope VGKAMYAPPISGQIR
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^{k}, H-2^{b}, H-2^{s}, H-2^{d})
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- This peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^{k}$, E^{k}), B10.D2 mice (H-$2A^{d}$, E^{d}), B10.A(5R) mice (H-$2A^{b}$, E^{b}), and B10.S(9R) mice (H-$2A^{s}$, E^{s})
- KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including VGKAMYAPPISGQIR and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (430–453)
Author Location gp120 (430–453)
Epitope VGKAMYAPPISGQIRCSSNITGLL
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (MHC) mouse (H-2^{b})
Keywords epitope processing
References Sjolander *et al.* 1996

- Study demonstrates that T-cell determinants from glycoproteins can depend on the glycosylation of the protein.
- Peptide stimulation of an *in vitro* proliferative response required *in vivo* priming with glycosylated protein.
- Local glycosylation sites thought not to be part of the epitope, but may be important for epitope processing.

HXB2 Location gp160 (432–451)
Author Location gp120 (432–451 IIIB)
Epitope KAMYAPPISGQIRCSSNITG?
Epitope name H4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 6.3.

HXB2 Location gp160 (433–447)
Author Location Env (UG92005)
Epitope AMYAPPIAGLIQCSS
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)

Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This epitope is located in the C4 region of UG92005 (UG, clade D) and was recognized by ten hybridomas with Vβ usage Vβ 6, 8.1, 8.2, 13, 14 and not determined – among the ND Vβ set, three Vαs were identified, Vα 2, 8, and 11.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (433–447)
Author Location Env (gp160) (UG92005)
Epitope AMYAPPIAGLIQCSS
Subtype D
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* Env *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H2b)
Assay type cytokine production, CD4 T-cell Elispot - IFNγ
Keywords vaccine-induced epitopes, variant cross-recognition or cross-neutralization, vaccine antigen design
References Zhan *et al.* 2004

- To develop a polyvalent Env vaccine, subtype specific B and D T-helper epitopes were identified, and mixtures of strain 1007, clade B, or UG92005, clade D envelopes were given to C57BL/6J mice. Mice were intramuscularly immunized with recombinant DNA, then intraperitoneally with rVV and finally with env protein in CFA. A dilution of 1/100 could still elicit type specific responses, and responses persisted with different prime boost combinations.
- T-cell hybridoma UGP2-17 was isolated from mice immunized with env sequence UG92005 (clade D), and it recognized the C4/V4 region peptide AMYAPPIAGLIQCSS. The minimal peptide recognized by 10007P3-23 was PPIAGLIQ, which matched only 5/8 residues in the B clade isolate, ppiRgQiK.
- Priming with 1007 and UG env's induced both Env-specific (SNNTVGNPIILPCRI and AMYAPPIAGLIQCSS) and cross-reactive (PKVSFEPIPIHYCAP, C2, GNIRQAHCNVSKAKW, V3-C3) Th responses in murine spleen cells.

HXB2 Location gp160 (436–451)
Author Location gp120 (IIIB)
Epitope APPIGGQISCSSNITY
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (438–460)
Author Location gp120 (443–465 NL43)
Epitope PISGQIRCSSNITGLLLTRDGGN
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* gp120, gp160
Species (MHC) human
References Sitz *et al.* 1999

- There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients.
- Close to 40% of vaccinees had a stimulation index of greater than 5 to this peptide.

HXB2 Location gp160 (439–448)
Author Location gp120 (151–160 W6.ID)
Epitope IGGQIRCSSN
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21
Species (MHC) human
References Jones *et al.* 1999

- HIV-1 specific T-cell lines isolated from an HIV seronegative volunteer vaccinated with rgp120 and a QS21/MPL adjuvant.
- One T-cell line responds to two overlapping peptides, and the region of overlap is IGGQIRCSSN.
- The IIIB version of the first reactive peptide, EVGKAMYAPPIGGQIRCSSN, has a single substitution and induces proliferation as well as the original W61D peptide: evgkamyappiSgqircssn.

HXB2 Location gp160 (439–461)
Author Location Env (438–460)
Epitope IRGQIRCSSNITGLLLTRDGGNN
Epitope name HIV_env_DRB0101_1
Subtype M

Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type T-cell Elispot
Keywords computational epitope prediction
References De Groot *et al.* 2004

- Bioinformatic tools (EpiMatrix and Conservatrix) were employed to predict 9 highly conserved and promiscuous class II restricted T helper epitopes from HIV-1 env sequences for a cross-clade polyepitope vaccine. 10/34 HIV-1 infected patients induced Th1 immune responses to 8/9 study peptides.
- 2/28 subjects tested responded to this peptide.
- Class II peptides containing putative epitopes were selected to favor DRB0101 presentation, as there is a transgenic mouse model for this allele for future vaccine studies. The highest scoring DRB0101 sequence within this peptide was QIRCSSNIT.

HXB2 Location gp160 (446–461)
Author Location gp120 (IIIB)
Epitope SSNITGLLLTRDGGTC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (452–471)
Author Location gp120 (452–471 IIIB)
Epitope LLLTRDGGNSNNESEIFRPG?
Epitope name I1
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 2/15 responders recognized this peptide, average SI = 3.5.

HXB2 Location gp160 (456–470)
Author Location gp120 (IIIB)
Epitope RDGGTNVTNDTEVFRC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (459–473)
Author Location gp120 (459–473 IIIB, B10)
Epitope GNSNNESEIFRPGGG
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (468–483)
Author Location gp120 (466–481)
Epitope FRPGGGDMRDNWRSEL
Immunogen HIV-1 infection
Species (MHC) human
References Krowka *et al.* 1990

- Conjugation of HIV peptides to liposomes and rIL-2 stimulation may enhance cell-mediated responses.

HXB2 Location gp160 (472–491)
Author Location gp120 (472–491 IIIB)
Epitope GGDMRDNWRSELYKYKVVKI?
Epitope name I3
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 2/15 responders recognized this peptide, average SI = 7.2.

HXB2 Location gp160 (474–488)
Author Location gp120 (474–488 IIIB, B10)
Epitope DMRDNWRSELYKYKV
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (476–490)
Author Location gp120 (483–497 IIIB)
Epitope RDNWRSELYKYKVVK
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{d, t4}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (476–490)
Author Location gp160 (483–497 IIIB)
Epitope RDNWRSELYKYKVVK
Immunogen Vaccine

Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^s)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- This peptide elicited proliferative responses in B10.BR mice (H-2A^k and B10.S(9R) mice (H-2A^s, E^s)
- RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes including RDNWRSELYKYKVVK and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (476–499)
Author Location gp160 (483–506 IIIB)
Epitope RDNWRSELYKYKVVKIEPLGVAPT
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) human, mouse (H-2^k, H-2^b, H-2^s, H-2^d)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide.
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people.
- This cluster peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s)
- IL-2 production in response to this peptide was observed in 52% (14/27) of asymptomatic HIV-infected individuals.

HXB2 Location gp160 (479–498)
Author Location gp120 (481–500 MN)
Epitope WRSELYKYKVVTIEPLGVAP
Epitope name 2013
Subtype B
Immunogen Vaccine
Vector/Type: DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) guinea pig
Keywords vaccine-specific epitope characteristics, Th1
References Chattergoon *et al.* 2002

- Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.
- A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.
- 0/5 animals vaccinated with rec gp120 responded by DTH to this peptide, while 6/6 vaccinated with plasmid gp120 DNA responded.

HXB2 Location gp160 (482–501)
Author Location gp120 (482–501 IIIB)
Epitope ELYKYKVVKIEPLGVAPTKA
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* Env
Species (MHC) macaque
References Lekutis *et al.* 1997

- HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkey.
- Epitope was recognized by both monkeys used in this study.

HXB2 Location gp160 (482–501)
Author Location gp120 (482–501 IIIB)
Epitope ELYKYKVVKIEPLGVAPTKA?
Epitope name I4
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 3/15 responders recognized this peptide, average SI = 6.0.

HXB2 Location gp160 (483–502)
Author Location gp120 (480–499 89.6)
Epitope LYKYKVVRIEPIGVAPTRAK
Epitope name Peptide 46
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in 7/10 BALB/c mice tested, and in only 1/10 CBA/J mice.

HXB2 Location gp160 (484–496)
Author Location gp120 (484–496 HXB2)
Epitope YKYKVVKIEPLGV
Subtype B
Immunogen Vaccine

Vector/Type: DNA *Strain:* B clade HXB2
HIV component: Env
Species (MHC) macaque (DR*W201)
References Lekutis & Letvin 1998

- Variants of this epitope with substitutions at position 490(K) retained ability to bind to MHC class II, but failed to induce proliferation/cytokine secretion in HIV-1 env-specific CD4+ Th cells.
- The modified peptide antagonized the wildtype peptide-induced proliferative response.

HXB2 Location gp160 (484–498)
Author Location gp120 (484–498 IIIB, B10)
Epitope YKYKVVKIEPLGVAP
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (484–499)
Author Location gp120 (492–506 IIIB)
Epitope CKYKVVKIEPLGVAPT
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{d, k, t4, i5}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (485–499)
Author Location gp160 (492–506 IIIB)
Epitope KYKVVKIEPLGVAPT
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^b, H-2^s, H-2^d)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- This peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)
- RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes including KYKVVKIEPLGVAPT and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (485–500)
Author Location gp120 (IIIB)
Epitope KYKVIKIEPLGIAPTC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (486–494)
Author Location gp120 (486–494 IIIB)
Epitope YKVVKIEPL
Immunogen SHIV infection
Species (MHC) macaque (DRB*W201)
References Lekutis & Letvin 1997

- C5 region minimal epitope determined through fine epitope mapping.

HXB2 Location gp160 (487–512)
Author Location gp120 (494–518 IIIB)
Epitope KVVKIEPLGVAPTKAKRRVVQREKRC
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (MHC) mouse
References Goodman-Snitkoff *et al.* 1990

- Identification of putative Th epitopes that stimulate an antibody response in peptide immunized mice.

HXB2 Location gp160 (492–512)
Author Location gp120 (492–512 IIIB)
Epitope EPLGVAPTKAKRRVVQREKRA?
Epitope name I5
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 1/15 responders recognized this peptide, SI = 4.9.

HXB2 Location gp160 (493–511)
Author Location gp120 (490–508 89.6)
Epitope PIGVAPTRAKRRTVQREKR
Epitope name Peptide 47
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6
HIV component: gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse
Donor MHC H-2k, H2-d
Keywords epitope processing, immunodominance
References Dai *et al.* 2001

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was reactive in only 2/10 BALB/c mice tested, and in 8/10 CBA/J mice.

HXB2 Location gp160 (499–511)
Author Location gp120 (IIIB)
Epitope TKAKRRVVEREKR
Immunogen in vitro stimulation or selection
Species (MHC) human (DR)
References Wilson *et al.* 1997b

- Thought to be a mimic of a HLA class II DR β chain variable region.
- Response to this epitope may cause a breakdown of self-tolerance.
- Presentation of epitope induced autoreactive T-cell lines in PBMC from uninfected donors.
- Suppression of proliferation to soluble antigens by the CD8+ fraction of TKAKRRVVEREKR stimulated T-cells was observed.

HXB2 Location gp160 (499–519)
Author Location gp41 (MN)
Epitope TKAKRRVVQREKRAAIGALF
Epitope name TF20
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords HAART, ART, acute infection
References Malhotra *et al.* 2003

- 92 acute- or early-HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy.
- This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail. These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintained in Env.

HXB2 Location gp160 (519–543)
Author Location Env (519–543)
Epitope FLGFLGAAGSTMGAASLTLTVQARC
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) macaque
References Nehete *et al.* 1993

- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice, and in rhesus monkeys.
- Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys.

HXB2 Location gp160 (519–543)
Author Location Env (519–543)
Epitope FLGFLGAAGSTMGAASLTLTVQARQ
Immunogen HIV-1 infection
Species (MHC) human, chimpanzee
References Nehete *et al.* 1998b

- HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env.

HXB2 Location gp160 (519–543)
Author Location gp41 (519–543)
Epitope FLGFLGAAGSTMGAASLTLTVQARC
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-$2^{bxk,\ sxd}$)
References Sastry & Arlinghaus 1991

- Peptides induced T-cell proliferative response to immunizing peptide and to gp160.

HXB2 Location gp160 (547–561)
Author Location gp41 (547–561 IIIB, B10)
Epitope GIVQQQNNLLRAIEA
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (562–576)
Author Location gp41 (562–576 IIIB, B10)
Epitope QQHLLQLTVWGIKQL
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (570–589)
Author Location gp41 (MN)
Epitope VWGIKQLQARVLAVERYLKD
Epitope name VD20
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DR)
Assay type cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
References Malhotra *et al.* 2003

- 92 acute- or early-HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy.
- This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail. The CD4+ clones showed MHC-restricted cytotoxicity and secreted high levels of cytokines when stimulated. These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR

clonal transcripts, and the epitope sequence being maintained in Env.
- This peptide showed promiscuous binding to DRB1*0101, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0801 DRB4*0101 DRB5*01.

HXB2 Location gp160 (572–591)
Author Location gp41 (572–591)
Epitope GIKQLQARILAVERYLKDQQ
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-$2^{d, b}$)
References Brown *et al.* 1995
- This peptide was a good immunogen in BALB/c and CBA mice, producing a strong proliferative response.
- At least one of the four residues GIKQ enhances stimulation, and in CBA mice these residues influence the ability to prime T-cells *in vivo*.
- QLQARILAVERY stimulated the greatest *in vitro* T-cell response.
- VERYLKDQQ was the minimal reactive sequence recognized by a T-cell line.

HXB2 Location gp160 (576–591)
Author Location gp41 (576–591)
Epitope LQARILAVERYLKDQQ
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-$2^{d, b}$)
References Brown *et al.* 1995
- This peptide was a poor immunogen in BALB/c and CBA mice used in this experiment, producing a weak proliferative response.

HXB2 Location gp160 (578–608)
Author Location gp41 (585–615 IIIB)
Epitope ARILAVERYLKDQQLLGIWGCSGKLICTTAV
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse
References Goodman-Snitkoff *et al.* 1990
- Identification of putative Th epitopes that can stimulate an antibody response in peptide immunized mice.

HXB2 Location gp160 (579–601)
Author Location gp41 (579–601)
Epitope RILAVERYLKDQQLLGGIWGCSGK
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) mouse (H-$2^{d, b}$)
References Brown *et al.* 1995
- This peptide was a good immunogen in BALB/c and CBA.
- This peptide produced a strong Th response in both mice strains which was more responsive towards GIKQLQARILAVERYLKDQQ and LQARILAVERYLKDQQ than to immunizing peptide.

HXB2 Location gp160 (579–604)
Author Location gp41 (584–609 LAI)
Epitope RILAVERYLKDQQLLGIWGCSGKLIC
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989
- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (586–597)
Author Location Env (586–598)
Epitope YLRDQQLLGIWG
Immunogen HIV-1 infection
Species (MHC) human, chimpanzee
References Nehete *et al.* 1998b
- HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env.

HXB2 Location gp160 (586–598)
Author Location Env (586–598)
Epitope YLRDQQLLGIWGC
Immunogen Vaccine
Vector/Type: peptide
Species (MHC) macaque, mouse
References Nehete *et al.* 1993
- Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice.
- Proliferative response to this peptide was observed in 1/3 immunized rhesus monkeys, with a weak transient response in the other two.

HXB2 Location gp160 (593–604)
Author Location gp41 (593–604 IIIB)
Epitope LGIWGCSGKLIC
Immunogen HIV-1 infection
Species (MHC) human
References Bell *et al.* 1992
- Elicits T-cell proliferation and B cell responses, but only during the asymptomatic phase of HIV infection.

HXB2 Location gp160 (593–604)
Author Location gp41 (598–609 LAV-1)
Epitope LGLWGCSGKLIC
Immunogen Vaccine

Species (MHC) mouse ($H2^{d}$)
References Schrier *et al.* 1988
- Murine T-dependent B-cell response – 7/29 had a proliferative response to this peptide.

HXB2 Location gp160 (594–603)
Author Location gp41 (594–603 IIIB)
Epitope GIWGCSGKLI
Immunogen HIV-1 infection
Species (MHC) human
References Kelleher *et al.* 1998b
- Epitope documented as a "previously described' epitope Bell *et al.* [1992], but in Bell *et al.* it was described as gp41(594-603 IIIB), LGIWGCSGKLIC.
- Immunization with a p24-VLP virus-like particle did not significantly impact CD4+ lymphocyte count, viral load, or p24 antibody titre.

- Immunization with p24-VLP did not increase the proliferative response to this gp41 epitope, however, there was a modest, short-lived increased proliferative response to p24.

HXB2 Location gp160 (594–604)
Author Location gp41 (consensus)
Epitope GIWGCSGKLIC
Immunogen HIV-1 infection
Species (MHC) human
References Mutch *et al.* 1994

- Core region of peptides that can stimulate proliferative responses from seronegative and seropositive people.

HXB2 Location gp160 (598–609)
Author Location gp41 (603–614 LAI)
Epitope CSGKLICTTAVP
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (604–615)
Author Location gp41 (609–620 LAI)
Epitope CTTAVPWNASWS
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (606–620)
Author Location gp41 (1035)
Epitope TNVPWNASWSNKSLE
Subtype B
Immunogen Vaccine
Vector/Type: vaccinia prime with gp120 boost *Strain:* B clade 1035 *HIV component:* Env *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (Class II I Ab)
Assay type T-cell Elispot
Keywords epitope processing, vaccine-induced epitopes, escape, TCR usage
References Zhan *et al.* 2003

- A very narrow Th response was stimulated in C57BL/6 mice vaccinated with vaccinia expressed HIV-1 env clone 1035, to the peptide PKVSFEPIPIHYCAP, located in the C2 region of gp120. The only other peptide recognized using Elispot on Env overlapping peptides to test vaccine responses in the mice was this one: TNVPWNASWSNKSLE, located in gp41.

HXB2 Location gp160 (606–620)
Author Location gp41 (UG92005)
Epitope TNVPWNASWSNKSLE
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This gp140 epitope of UG92005 (UG, clade D) was recognized by five hybridomas with Vβ usage Vβ 8.1, 14 and not determined – one of the Vβ 8.1 was shown to utilize Vα 8.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (609–616)
Author Location gp41 (consensus)
Epitope PWNASWSN
Immunogen HIV-1 infection
Species (MHC) human
References Mutch *et al.* 1994

- Core region of peptides that can stimulate proliferative responses from seronegative and seropositive people.

HXB2 Location gp160 (611–620)
Author Location gp41 (1007, UG92005)
Epitope NASWSNKSLE
Immunogen Vaccine
Vector/Type: DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2 IA^b)
Keywords inter-clade comparisons, epitope processing, TCR usage
References Surman *et al.* 2001

- This gp41 epitope is conserved in 1007 (US, clade B) and UG92005 (UG, clade D) and was recognized by two hybridomas from two different mice that were vaccinated with different clades – the Vβ usage was Vβ 4 and 14.
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (T[TN]VPWNASWSNKSLE and NASWSNKSLEQIWNN) – the only difference between 1007 and UG92005 for these two proteins is that 1007 has a T and UG92005 has an N in the second position of the first peptide.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

HXB2 Location gp160 (614–629)
Author Location gp41 (IIIB)
Epitope WSNKSLEDIWDNMTWC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (634–649)
Author Location gp41 (IIIB)
Epitope EIDNYTNTIYTLLEEC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (647–661)
Author Location gp41 (647–661 IIIB, B10)
Epitope EESQNQQEKNEQELL
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (650–662)
Author Location gp41 (655–667 LAI)
Epitope QNQQEKNEQELLE
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (667–681)
Author Location gp41 (667–681 IIIB, B10)
Epitope ASLWNWFNITNWLWY
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (682–696)
Author Location gp41 (682–696 IIIB, B10)
Epitope IKLFIMIVGGLVGLR
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a

- 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

HXB2 Location gp160 (724–745)
Author Location gp41 (731–752)
Epitope PRGPDRPEGIEEEGGERDRDRS
Immunogen Vaccine
Vector/Type: peptide in cowpea mosaic virus (CPMV) *HIV component:* gp41 *Adjuvant:* Quillaja saponin (Quil-A)
Species (MHC) mouse (H-2^k)
Keywords Th1
References McInerney *et al.* 1999

- A gp41 peptide was expressed in a cowpea mosaic virus (CPMV) and mice were vaccinated with a purified chimeric particle – out of five adjuvants tested, only Quil A could stimulate anti-gp41 antibodies and an *in vitro* proliferative response.
- The antibodies were predominantly IgG2a, suggesting a Th1 response.

HXB2 Location gp160 (732–744)
Author Location gp41 (737–749 LAI)
Epitope GIEEEGGERDRDR
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References Schrier *et al.* 1989

- Stimulates T-cell proliferation in HIV-infected donors.

HXB2 Location gp160 (780–794)
Author Location gp41 (787–801 IIIB)
Epitope RIVELLGRRGWEALK
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{d, k, t4}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (780–794)
Author Location gp160 (787–801 IIIB)
Epitope RIVELLGRRGWEALK
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^d, H-2^s)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), and B10.S(9R) mice (H-$2A^s$, E^s)
- RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including RIVELLGRRGWEALK and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^k mice.

HXB2 Location gp160 (780–813)
Author Location gp160 (787–820 IIIB)
Epitope RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide.
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people.
- This cluster peptide elicited proliferative responses in cells from only B10.BR mice (H-$2A^k$, E^k), and not from B10.D2 mice (H-$2A^d$, E^d), B10.A(5R) mice (H-$2A^b$, E^b), or B10.S(9R) mice (H-$2A^s$, E^s)
- IL-2 production in response to this peptide was observed in 59% (17/29) of asymptomatic HIV-infected individuals.

HXB2 Location gp160 (794–808)
Author Location gp41 (801–815 IIIB)
Epitope KYWWNLLQYWSQELK
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2^k)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (794–808)
Author Location gp160 (801–815 IIIB)
Epitope KYWWNLLQYWSQELK
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^d, H-2^s)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), and B10.S(9R) mice (H-$2A^s$, E^s)
- RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including KYWWNLLQYWSQELK and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^k mice.

HXB2 Location gp160 (799–813)
Author Location gp41 (806–820 IIIB)
Epitope LLQYWSQELKNSAVS
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{k, d, t4}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (799–813)
Author Location gp41 (806–820 IIIB)
Epitope LLQYWSQELKNSAVS
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{k, d, t4}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (799–813)
Author Location gp160 (806–820 IIIB)
Epitope LLQYWSQELKNSAVS
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^d, H-2^s)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), and B10.S(9R) mice (H-$2A^s$, E^s)
- RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including LLQYWSQELKNSAVS and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^k mice.

HXB2 Location gp160 (814–829)

Author Location gp41 (IIIB)
Epitope WLNATAIAVTEGTDRC
Immunogen in vitro stimulation or selection
Species (MHC) human
References Manca *et al.* 1995b

- Peptide stimulation of PBMC from non-infected individuals *in vitro*.
- Peptide priming does not always induce T-cells that recognize whole protein.

HXB2 Location gp160 (821–835)
Author Location gp41 (828–842 IIIB)
Epitope AVAEGTDRVIEVVQG
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2^k)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (821–835)
Author Location gp160 (828–842 IIIB)
Epitope AVAEGTDRVIEVVQG
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^b, H-2^s)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)
- AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER encompasses several murine Th epitopes including AVAEGTDRVIEVVQG and is referred to as a "multideterminant region" or cluster peptide.

HXB2 Location gp160 (821–838)
Author Location gp41 (827–843)
Epitope YVAEGTDRVIEVVQGACR
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression
References Caruso *et al.* 1997

- As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71.
- The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost.
- This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24.

HXB2 Location gp160 (821–853)
Author Location gp160 (828–860 IIIB)
Epitope AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) human, mouse (H-2^k, H-2^b, H-2^s, H-2^d)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide.
- Six multideterminant region cluster peptides were evaluated for Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people.
- This cluster peptide elicited proliferative responses in cells from all four MHC types tested: B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)
- IL-2 production in response to this peptide was observed in only 8% (1/12) of asymptomatic HIV-infected individuals.

HXB2 Location gp160 (827–835)
Author Location gp41 (834–842 IIIB)
Epitope DRVIEVVQG
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2^k)
References Hale *et al.* 1989

- Suggested H-2^k epitope based on region of overlap.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4
Immunogen Vaccine
Vector/Type: peptide prime with protein boost *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) macaque
References Hosmalin *et al.* 1991

- Peptide priming to induce T-cell help enhances antibody response to gp160 immunization.
- Called Th4.1 and TH4.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1997

- used in a study of the influence of pentoxifylline on HIV specific T-cells.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4
Immunogen
Species (MHC) human
References Pinto *et al.* 1995

- CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers.
- Called Th4.1 and TH4.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1991a

- Peptides stimulate Th cell function and CTL activity in similar patient populations.
- Called Th4.1 and TH4.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp160
Species (MHC) human
References Clerici *et al.* 1991b

- Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection.
- Called Th4.1 and TH4.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4
Immunogen
Species (MHC) human
References Clerici *et al.* 1992

- Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men.
- Called Th4.1 and TH4.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4
Immunogen HIV-1 infection
Species (MHC) human
References Clerici *et al.* 1989

- IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals.
- Called Th4.1 and TH4.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4
Immunogen HIV-1 infection
Species (MHC) human
References Kaul *et al.* 1999

- Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases)
- Helper epitopes used in this study were noted to be previously described Clerici *et al.* [1989], and were not explicitly described in Kaul *et al.* [1999]

HXB2 Location gp160 (827–841)
Author Location gp41
Epitope DRVIEVVQGAYRAIR
Epitope name TH4, Th4.1
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC) human
Keywords inter-clade comparisons, responses in children, mother-to-infant transmission
References Kuhn *et al.* 2001a

- In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4.
- The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents.
- 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breastfeeding.
- Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.

HXB2 Location gp160 (827–841)
Author Location Env (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4.1
Immunogen HIV-1 infection, HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
Keywords mother-to-infant transmission
References Clerici *et al.* 1993a

- Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected.
- PBL from 10/21 of the mother showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.

HXB2 Location gp160 (827–841)
Author Location Env (IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4.1
Subtype B
Immunogen HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
References Clerici *et al.* 1994a

- Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection.
- Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.

HXB2 Location gp160 (827–841)
Author Location HIV-1 (IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4.1
Subtype B
Immunogen HIV-1 infection
Species (MHC)
Assay type cytokine production
References Clerici *et al.* 1994b

- IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.

HXB2 Location gp160 (827–841)
Author Location Env (834–848)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4-1
Immunogen HIV-1 infection
Species (MHC) human
Assay type proliferation
Keywords responses in children, mother-to-infant transmission
References Kuhn *et al.* 2001b

- Th proliferative responses in cord blood at delivery to a cocktail of HIV envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery.
- The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).

HXB2 Location gp160 (827–841)
Author Location Env (gp160) (421–436)
Epitope DRVIEVVGQAYRAIR
Epitope name TH4.1
Subtype C
Immunogen HIV-1 infection
Species (MHC) human
Country South Africa.
Assay type proliferation
Keywords responses in children, variant cross-recognition or cross-neutralization
References Meddows-Taylor *et al.* 2004

- Viral isolates (gp160) from 16 vertically HIV-1 infected children (8 T-helper cell Env responders and 8 non-responders) were analyzed for variation after comparison with Env peptide sequences (conserved regions T1, T2 and TH4.1, hypervariable regions P18 MN and P181 IIIB) used for in vitro stimulation.
- No correlation between the age, clinical category (mild or severe), HIV-1 viral load and the degree of epitope variation was established.

HXB2 Location gp160 (827–841)
Author Location gp41 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Epitope name TH4
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{k,\ i5}$)
References Hale *et al.* 1989

- Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.
- Called Th4.1 and TH4.

HXB2 Location gp160 (827–841)
Author Location gp160 (834–848 IIIB)
Epitope DRVIEVVQGAYRAIR
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^b)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a

- This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k) and B10.A(5R) mice (H-$2A^b$, E^b)

HXB2 Location gp160 (827–853)
Author Location Env (HIV-1 IIIB)
Epitope DRVIEVVQGAYRAIRHIPRRIRQGLER
Subtype B
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB, SIV *HIV component:* Env, Gag, Pol *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72), Montanide (ISA 51)
Species (MHC) macaque
Assay type proliferation
Keywords mucosal immunity
References Belyakov *et al.* 2001

- Different HIV strains were used for different regions: env HIV-1 IIIB, gag SIV, pol SIV
- Intrarectal vaccination with a Th and CTL peptide vaccine provided better protection against intrarectal challenge with pathogenic SHIV-Ku1 than subcutaneous administered vaccine. In some animals after the initial viremia, viral loads were diminished to undetectable levels in the blood and intestine, and CD4+ T cells were better preserved.
- The CD4 T-cell proliferative response correlated with the level of the CTL response.

HXB2 Location gp160 (829–843)
Author Location gp160 (836–850 IIIB)
Epitope VIEVVQGAYRAIRHI
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^b)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a
• This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k) and B10.A(5R) mice (H-$2A^b$, E^b)

HXB2 Location gp160 (834–841)
Author Location gp41 (841–848 IIIB)
Epitope QGAYRAIR
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2^{i5})
References Hale *et al.* 1989
• Suggested H-2^k epitope based on region of overlap.

HXB2 Location gp160 (834–848)
Author Location gp41 (841–855 IIIB)
Epitope QGAYRAIRHIPRRIR
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{d, t4, i5}$)
References Hale *et al.* 1989
• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (834–848)
Author Location gp160 (841–855 IIIB)
Epitope QGAYRAIRHIPRRIR
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (H-2^k, H-2^b, H-2^d, H-2^s)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a
• This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k), B10.A(5R) mice (H-$2A^b$, E^b), B10.D2(H-$2A^d$, E^d), and B10.S(9R) mice (H-$2A^s$, E^s)

HXB2 Location gp160 (839–848)
Author Location gp41 (846–855 IIIB)
Epitope AIRHIPRRIR
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{d, t4}$)
References Hale *et al.* 1989
• Suggested H-$2^{d,t4}$ epitope based on region of overlap.

HXB2 Location gp160 (839–853)
Author Location gp41 (846–860 IIIB)
Epitope AIRHIPRRIRQGLER
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-$2^{d, t4}$)
References Hale *et al.* 1989
• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.

HXB2 Location gp160 (839–853)
Author Location gp160 (828–842 IIIB)
Epitope AIRHIPRRIRQGLER
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) human, mouse (H-2^k, H-2^b, H-2^s)
References Berzofsky *et al.* 1991b; Berzofsky *et al.* 1991a
• This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)

HXB2 Location gp160 (842–856)
Author Location gp41 (842–856 IIIB, B10)
Epitope HIPRRIRQGLERILL
Immunogen HIV-1 infection
Species (MHC) human
References Wahren *et al.* 1989b; Wahren *et al.* 1989a
• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.

III-B-15 Env Helper, CD4+, T-cell epitopes

HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* gp120, gp160
Species (MHC) mouse
Keywords Th1
References Shiver *et al.* 1997
• DNA vaccinations of BALBc mice with a gp120 or gp160 DNA vaccine elicited a strong T-cell proliferative response with Th1-like secretion of γ interferon and IL-2, with little or no IL-4, as well as antigen specific gp120 Abs.
• An intramuscular route of inoculation gave a stronger proliferative response than intradermal.
• A proliferative response could be detected in all lymph tissues tested: spleen, PBMC, and mesenteric, iliac, and inguinal lymph nodes.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Gag, gp160, Pol *Adjuvant:* CD86
Species (MHC) mouse
References Kim *et al.* 1997d
• A gp160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecule CD86, gives an increase in the proliferative responses to gp120 in mice.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen
Species (MHC) human
References De Berardinis *et al.* 1997

- Sequences flanking helper T-cell immunogenic domains can be important for immunogenicity.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Rosenberg *et al.* 1997

- A strong proliferative response to p24 and gp160 was found in a healthy long term survivor.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) macaque
Keywords Th1, Th2
References Kent *et al.* 1997b

- Macaca nemestrina can be infected with HIV, and clear the infection within 6 months, so it is of interest to examine their initial immune response.
- A strong proliferative response against gp160 with IL-4 production, indicating a Th2 response, was found with 4 weeks of infection.
- The gp160 proliferative response by 8 weeks produces both IL-4 and γ interferon, indicating both Th1 and Th2 responses.

HXB2 Location Env
Author Location gp120 (HXBc2)
Epitope
Immunogen Vaccine
Vector/Type: DNA prime with gp160 boost *Strain:* B clade HXBc2 *HIV component:* gp160
Species (MHC) macaque
References Letvin *et al.* 1997

- Vaccination of Macaca mulatta (rhesus monkeys) with a HXBc2 env DNA prime and a protein boost elicited a T-cell proliferative response, a CTL response, and type-specific neutralizing antibodies.
- Vaccinated animals challenged with SHIV-HXB2 were protected from infection.

HXB2 Location Env
Author Location gp120 (MN)
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA *Strain:* B clade MN *HIV component:* Env, Rev
Species (MHC) human
References MacGregor *et al.* 1998

- An HIV DNA env and rev vaccine given to 15 asymptomatic HIV+ individuals at three different dosages, 30, 100 or 300 μg, was safe.
- All three groups showed an increased proliferative response after vaccination.

HXB2 Location Env
Author Location Env
Epitope
Immunogen
Species (MHC) human
References Mazzoli *et al.* 1997

- Study of HIV-specific immunity in seronegative partners of HIV-positive individuals – Env peptides could stimulate IL-2 production in 9/16 HIV-exposed seronegative individuals, and only 1/50 low-risk controls.
- Exposed-uninfected produced more IL-2 and less IL-10 then HIV-infected individuals.
- 8/9 of those whose PBMC produce IL-2 in response to Env peptides had concomitantly detected urinary or vaginal tract anti-HIV IgA.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Plana *et al.* 1998

- Patients from later stages of infection given HAART do not show restoration of HIV-1 specific Th proliferative responses.

HXB2 Location Env
Author Location Env
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Kelleher *et al.* 1998a

- Env and gag Th epitopes were pooled and used to test Th proliferative responses after IL2 therapy – while IL2 therapy causes an increase in CD4+ lymphocyte count, it does not increase HIV-1 specific proliferative responses.

HXB2 Location Env
Author Location gp160
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *HIV component:* gp160
Species (MHC) human
References Ratto-Kim *et al.* 1999

- Vaccinations with rgp160 did not enhance Th immunoproliferative responses in individuals who were immunized every 2 months for 5 years starting early in infection.

HXB2 Location Env
Author Location gp160
Epitope
Immunogen HIV-1 infection, Vaccine

Vector/Type: protein *HIV component:* gp160
Species (MHC) human
Keywords inter-clade comparisons
References Leandersson *et al.* 2000

- 27 HIV subtype B, 4 subtype C, 2 D and one of each subtype E, F, G infected individuals were either given rgp160 B clade immunizations or placebo. All rgp160 immunized individuals showed increased proliferation responses to the B clade immunizing antigen rgp160.
- gp120 was prepared from A, B, C, D, and E subtype virions and used as antigenic stimulus – 7 of 10 tested individuals responded to native gp120 from at least one additional subtype in addition to B subtype, while a placebo recipient did not respond to any gp120.
- This study shows that cross-subtype HIV-specific T-cell proliferative responses can be stimulated in patients already infected with another HIV-1 subtype – all immunized subjects could respond to the subtype B immunogen, but many developed responses to at least one more subtype.

HXB2 Location Env
Author Location gp160 (MN)
Epitope
Immunogen Vaccine
Vector/Type: gp160 prime with gp120 boost *Strain:* B clade MN *HIV component:* gp120, gp160
Species (MHC) human
Keywords Th1, Th2
References Gorse *et al.* 1999a

- Helper T-cell memory responses were induced by MN rgp160 as measured by proliferation and Th1 and Th2 cytokine release – this response could be boosted by MN rgp120.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen Vaccine
Vector/Type: fowlpoxvirus, ISCOM *Strain:* B clade SF2 *HIV component:* gp120
Species (MHC) macaque
Keywords Th1, Th2
References Heeney *et al.* 1998b

- Vaccinated monkeys with the highest level of Th1 and Th2 responses and the highest levels of NAbs were protected against a SHIV SF13 challenge – the ISCOM strategy gave more potent anti -gp120 responses than the Fowl pox strategy.
- When animals were challenged 4 months after boost, those that maintained high levels of HIV-1 specific IFNγ responses, indicative of a Th 1 response, were still protected.

HXB2 Location Env
Author Location (IIIB)
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* Env, Rev
Species (MHC) human
References Boyer *et al.* 1999

- A DNA vaccine containing env and rev was tested for safety and immune response in 15 HIV+ asymptomatic individuals.
- Enhanced proliferative activity and higher levels of MIP-1 alpha were detected in multiple study subjects.

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* GM-CSF/ENV chimera
Species (MHC) mouse
References Rodríguez *et al.* 1999

- A chimeric GM-CSF-env antigen expressed in a vaccinia vector elicits a higher HIV-specific env cellular immune response than when native env is used.

HXB2 Location Env
Author Location Env (LAI)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA prime with vaccinia boost *Strain:* B clade LAI *HIV component:* Env, Gag
Species (MHC) macaque
Keywords Th1, Th2
References Kent *et al.* 1998

- Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T-cell immunity than either vaccine alone.
- The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen Vaccine
Vector/Type: DNA, protein, virus-like particle (VLP), ISCOM
Species (MHC) macaque
Keywords Th1, Th2
References Heeney *et al.* 1999

- Ten different vaccine strategies were evaluated for their ability to protect from infection in a rhesus macaque model using a non-pathogenic SHIV challenge. Protection correlated with the magnitude of NAb responses, beta-chemokines, and a balanced Th response. DNA, protein+adjuvant, VLP and ISCOM vaccines were tested.
- HIV-1/ISCOMS gave the highest NAb titers, Th1 and Th2 responses, was the only vaccine formulation tested with a detectable CTL response, and gave enhanced beta-chemokine production.

HXB2 Location Env

Author Location gp160 (MN)
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp160
Species (MHC) human
References Kundu *et al.* 1998a

- This study followed 10 HLA-A2 asymptomatic HIV+ individuals as they received MN gp160 vaccinations over a two year period.
- There was an increased lymphoproliferative response but this did not impact viral load or CTL response.

HXB2 Location Env
Author Location gp120 (SF2)
Epitope
Immunogen Vaccine
Vector/Type: DNA, protein, ISCOM *Strain:* B clade SF2 *HIV component:* gp120 *Adjuvant:* MF59
Species (MHC) macaque
References Verschoor *et al.* 1999

- 16 rhesus Macaques were vaccinated with either an epidermal SF2 gp120 DNA vaccine, rgp120 with a MF59 adjuvant, or rgp120 incorporated into ISCOMs.
- DNA vaccination elicited a weak Th type 1 response and low antibody response, rgp120/MF59 triggered a strong antibody response, and rgp120/ISCOM induced both kinds of Th cells, and a strong humoral response.
- Animals were challenged with SF13 SHIV. Early induction of Th type 1 and type 2 responses with the rgp120/ISCOM vaccine provided the most effective immunity, protecting from infection.

HXB2 Location Env
Author Location Env (MN)
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade MN *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86
Species (MHC) mouse
References Kim *et al.* 1998

- Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.

HXB2 Location Env
Author Location Env (LAI, MN)
Epitope
Immunogen Vaccine
Vector/Type: canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease
Species (MHC) human
References Salmon-Ceron *et al.* 1999

- A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy uninfected volunteers.

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine
Vector/Type: DNA *Strain:* ZF1 *HIV component:* complete genome
Species (MHC) macaque
References Akahata *et al.* 2000

- Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging.
- Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153)
- 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected.
- PBMC from all vaccinated monkeys produced IFNγ, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response.
- 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit.
- 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit.

HXB2 Location Env
Author Location gp120 (W6.ID)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Zhang *et al.* 2001b

- T-helper cell proliferative responses to HIV p24, p55 and gp120 were tested in 27 patients with HIV infection – vigorous responses directed at Gag were detected in ten patients, but an Env specific response was detected in only one patient.

HXB2 Location Env
Author Location gp160
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Blazevic *et al.* 2000

- Prolonged viral suppression resulting from potent antiretroviral therapy did not allow an HIV T helper response to p24 or gp160, but Th proliferative responses to influenza, alloantigen, and PHA did develop in many HIV+ patients, and asymptomatic patients had stronger and more frequent Th response recovery than AIDS patients.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection

Species (MHC) human
Keywords HAART, ART
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *HIV component:* gp120
Species (MHC) human
Keywords Th1, Th2
References Sabbaj *et al.* 2000

- Proliferative responses in PBMC of uninfected individuals that were vaccinated with canarypox vector expressing HIV-1 antigens (ALVAC-HIV) and boosted with a recombinant gp120 subunit vaccine gave a Th1 and Th2 proliferative response upon stimulation with HIV-1 Env.
- All vaccinees produced IFNγ and IL10, most also produced IL-2, IL-6, IL-4 and IL-5.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp120
Species (MHC) human
Keywords Th1
References Hladik *et al.* 2001

- 16/29 HIV-1 infected and 24/30 vaccinated individuals had DTH reactions within 48 hours after an intradermal rec gp120 injection. Of nine DTH positive individuals, none had detectable proliferative responses. Thus skin testing may be a sensitive way to identify people with Th recall responses to vaccines, or in the absence of lymphoproliferaion.
- No 48 hour DTH responses were detected among uninfected volunteers, although 10/35 (40%) of the high risk and 11/32 (34%) of the low risk individuals developed an induration resembling DTH after 7-12 days, that may be indicative of primary induction of HIV-1 specific Th1-immunity.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1, Th2
References Wilson *et al.* 2000b

- Dysfunction of HIV-1 specific proliferative responses, but not responses to other antigens, is evident in HIV-1 progressive disease.
- Vigorous HIV-1 specific responses to p24, Nef and gp120 with SI between 8-99 were seen in 6/7 long term non-progressors (LTNP), the seventh had a borderline responses. IL-2 production was seen in all cases, and IL-4 production was also evident many responses.
- None of the progressors (0/5) had HIV-1 specific proliferative responses, or IL-2 or IL-4 induction.
- Non-HIV antigens (cytomegalovirus, PPD, Staphylococcus enterotoxin B, tetanus toxoid) gave similar responses in HIV-1 + LTNP, progressors, and HIV-1 controls.

HXB2 Location Env
Author Location gp160
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1
References Kalams *et al.* 1999a

- The strength of p24 specific Gag proliferative responses (SIs) were inversely correlated with viral load in 21 ARV naive patients. The responses were Th1, IFNgamma producing.
- Proliferative responses against gp160 were rarely observed (only 4 cases).

HXB2 Location Env
Author Location Env
Epitope
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade MN *HIV component:* Env, Rev *Adjuvant:* Bupivacaine
Species (MHC) human
Keywords early-expressed proteins
References MacGregor *et al.* 2002

- A phase I clinical trial of a HIV-1 Env and Rev DNA vaccine with a CMV promoter was conducted and Th proliferative, CTL and Elispot responses monitored. The construct was modified for safety and included no LTRs or packaging signals. The vaccine strategy was safe, and elicited strong CD4-T cell responses, but not CD8 T-cell responses. Rev elicited strong Th responses, and is a early produced protein so may confer advantages.
- With a 300 ug dose, 4/6 individuals had a lymphocyte proliferation (LP) responses to gp120, 3/6 to Rev.
- With a 1000 ug dose, 4/6 individuals had a LP and 2/6 had IFNgamma Elispot responses to gp160; 3/6 had LP, and 4/6 had IFNgamma Elispot responses to Rev.
- No responses to three specific CTL epitopes were observed by Elispot in individuals with appropriate HLA. Some cytotoxic activity against whole protein was observed that was CD4+ T-cell mediated.

HXB2 Location Env
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Clerici *et al.* 2002b

- Specific immunity was compared in a two-year study of chronically HIV-1 infected i) HAART-naive patients who were not progressing and had strong immune responses, ii) newly treated patients followed for 24 months after initiation of HAART, iii) and long-term HAART patients who had been on HAART at least 12 months prior to the study.
- HAART naïve patients had strongest proliferative responses at time zero, but long-term HAART patients the most significant increase in specific responses over the two year study period against HIV-1 gp160, influenza, and Candida. Similarly, IL-2 and IFNγ production in responses to gp160 was highest in the naïve group at time zero, but increased the most in the long-term HAART treated patients.
- Short-term HAART patients showed a significant improvement in their CD4+ T cell count and a reduction of plasma viremia, and had augmented IL-7 production, which was slightly reduced in long-term HAART patients.

HXB2 Location Env
Author Location gp160
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Palmer *et al.* 2002

- CD4+ T cell proliferative responses from 33 HIV-1 infected patients with HAART suppression were compared to 19 patients with active viral replication (HAART failures and HAART naive). Patients with HAART suppression showed stronger p24- and p66-specific proliferative responses compared to patient groups with active HIV-1 replication, suggesting active viral replication *in vivo* specifically reduces proliferation responses.
- gp160 proliferation responses were apparent in 7/32 donors tested, but weaker overall, with a median value for the suppressed group not above that found for HIV seronegative controls.
- No differences in the frequency of HIV-specific CD4+ T-cells that were positive for cytokine secretion in a flow cytometry assay were found in the HAART suppressed group versus the group with active viral replication.

HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

- Th proliferative responses were studied in 36 asymptomatic HIV-1 + patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- 4/15 responders recognized this peptide, average SI = 4.4.

HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Immunogen HIV-1 infection
Species (MHC) human
References Geretti *et al.* 1994

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HXB2 Location Env
Author Location gp120 (SF2)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, rate of progression
References Imami *et al.* 2002b

- 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile.
- In a comparison of responses to HIV-1 proteins based on 10 non-progressors, 3 immunologically discordant, and 70 progressors, SIs were always much higher for non-progressors and immunologically discordant than progressors. Among the non-progressors, the responses to different antigens were greater using p24 peptides than native p24. Native p24, Nef, gp120 proteins, and Remune (gp120 depleted HIV-1, p24 is subtype G), had roughly comparable distributions of SI values from the non-progressors, Nef and gp120 responses were somewhat diminished in immunologically discordant patients.

HXB2 Location Env
Author Location (BRU)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade BRU *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse
References Haas *et al.* 1991

- Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus.
- B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.

HXB2 Location Env
Author Location gp120 (HIV-1,IIIB)
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC) human
Assay type cytokine production
Keywords HIV exposed persistently seronegative (HEPS)
References Fowke *et al.* 2000

- A cohort of Nairobi sex-worders were defined to be resistant to infection by virtue of remaining seronegative despite repeated high risk exposure. 24 were tested for HIV specific T-helper responses detemined by IL-2 production *in vitro* in response to gp120 peptides or soluble gp120 protein.
- In 7/17 resistant women showed IL-2 stimulation >= 2.0, and specific CTL responses were detected in 15/22 resistant women. 0/12 of the control low-risk subjects had detecatble T-cell responses.

HXB2 Location Env
Author Location gp160
Epitope
Immunogen HIV-1 infection, Vaccine *Vector/Type:* protein *HIV component:* gp160 *Adjuvant:* aluminum phosphate
Species (MHC) human
Assay type proliferation
Keywords HAART, ART, immunotherapy
References Hejdeman *et al.* 2003

- Groups of ten asymptomatic HAART-treated HIV-1 + patients with undetected viral loads were monitored for two years after i) no immunization, ii) immunization with rgp160, or iii) immunization with tetanus. Ten HIV-1- volunteers were immunized with tetanus as a control. Results were compared with an rgp160 group tested before HAART was available. The HAART-treated group had increased magnitude and duration of proliferative response to rgp160, maintaining the response for the two year study period. CD4 T-cell responses to tetenus were also improved in the HAART group.
- The recall response to tetanus toxoid and tuberculin were boosted by the rgp160 immunization, particularly in the HAART-treated group.

HXB2 Location Env
Author Location
Epitope
Immunogen HIV-1 exposed seronegative
Species (MHC)
Assay type cytokine production
Keywords HIV exposed persistently seronegative (HEPS), acute infection, early treatment
References Puro *et al.* 2000

- This was a case report of a health care worker who had an percutaneous injury and exposure to HIV, and was immediatedly given combination therapy. The individual remained HIV Ab negative, but had tranisiently detectable viral RNA 2-3 weeks after the exposure. 58 weeks after exposure a Th response was detected by IL-2 production in response to HIV Env peptides.

HXB2 Location Env
Author Location
Epitope
Immunogen Vaccine *Vector/Type:* fowlpoxvirus, DNA prime with virus-like particle (VLP) boost *Strain:* B clade 89.6 *HIV component:* Env, Gag-Pol
Species (MHC) rabbit
Assay type cytokine production
Keywords Th1, Th2
References Radaelli *et al.* 2003

- Rabbits were immunized with fowlpox recombinant vectors or expression plasmids, which express either SIVmac239 gag/pol or HIV-1 env 89.6P genes, and then boosted with virus-like particles (VLPs)(gag/pol SIV with HIV env 89.6).
- A lymphoproliferative Th0 profile response and homologous neutralizing Ab were seen in all three groups. The pcDNA3gag/pol SIV construct was more efficient at producing Abs than the fowlpox construct, although the fowlpox env89.6 construct elicited good humoral and cellular responses. VLP boosting was shown to be efficacious; the pseudoviral structure of the VLP providing a more natural protein conformational was considered helpful for eliciting long term memory cells.

HXB2 Location Env
Author Location gp160
Epitope
Subtype B
Immunogen HIV-1 infection, Vaccine *Vector/Type:* canarypox prime with gp160 boost *Strain:* B clade MN/LAI-2 *HIV component:* gp160
Species (MHC) human
Assay type proliferation
Keywords vaccine-specific epitope characteristics, vaccine-induced epitopes
References Ratto-Kim *et al.* 2003

- The CD4+ T-helper response to vaccinees given ALVAC-HIV(vCP205) alone, rgp160 MN/LAI-2 alone, or the two combined in a prime-boost was investigated by establishing T cell lines and comparing proliferative responses to a series of peptides (15 mers overlapping by 10) spanning autologous gp160 MN/LAI-2. Th responses against Env during natural HIV-1 infection were also studied.
- Broad, strong T-helper responses scattered across the Env were obtained from volunteers who received a prime boost vCP205 + rgp160MN/LAI-2, while those receiving rgp160 responded to fewer peptides, and vCP205 to very few peptides.
- HIV-1 + volunteers had less breadth and amplitude of Th responses than vaccinees that got the prime-boost vaccine, although T-cell lines were readily generated from HIV+ individuals. Some vaccinees targeted C1 and C5, while infected individuals did not, and some infected individuals targeted V3, while vaccinees did not.
- The authors note that the differences in response may be contributed to by the fact the peptides used to screen the responses were the same as the vaccine strain, and different than the strains in the natural infection, but that there also may be real immunological differences in the two scenarios of vaccine verses natural infection.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC)
Assay type proliferation
Keywords HAART, ART
References Sullivan *et al.* 2003

- Lymphoproliferative responses to HIV antigens p24, gp120 and Nef were enhanced in eight patients who were switched from protease inhibitors to non-nucleoside reverse transcriptase inhibitors.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type cytokine production, proliferation
Keywords HAART, ART
References Hardy *et al.* 2003

- Upon initiating HAART, CD4+ T cell proliferative responses in 36 patients were restored to specific antigens, mitogens, and IL-2. Restored recall responses were largely to persistent antigens, and not to HIV-1 or new antigens, and recall responses were associated with IL-2, not IL-4 production.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords review, Th1, Th2, immune dysfunction
References Becker 2004b

- The review suggests HIV-1 shed gp120 virions can act as an allergen, inducing Th2 cytokine production, in particular IL-4, by Fc epsilon RI+ hematopoietic cells. This could inhibit IgG production and CTL responses, and inactivate Th1 cells. New vaccination strategies employing IL-4 inhibitors and anti-allergen drugs are discussed.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords review, Th1, Th2, immune dysfunction
References Becker 2004a

- Review raises the possiblity that the switch from Th1 to Th2 activity along with an increase in IL-4 and IgE production in HIV-1 infected patients are an allergic response to HIV-1 protein gp120. Alternative treatments to block Th2 cytokine production, e.g with Il-4 receptor inhibitors, are discussed.

HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: peptide, heat-shock protein (HSP70) *Strain:* B clade IIIB *HIV component:* gp120
Species (MHC) macaque
Assay type cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, T-cell Elispot
Keywords genital and mucosal immunity, vaccine antigen design
References Bogers *et al.* 2004

- Macaques were given vaginal or iliac lymph node immunizations with a novel peptide vaccine composed of SIV p27, CCR5, and N-terminal gp120 fragment, and hsp70 as a carrier.
- 5/8 SHIV 89.6P challenged macaques were protected from infection and vaccinated animals had higher CD4+ T cell numbers than non-vaccinated controls. T-cell proliferation in responses to gp120, vaginal IgG and IgA Abs, and cells producing IL-2, IL-4, and IFNgamma were increased in vaccinated animals.

HXB2 Location Env
Author Location gp160 (IIIB)
Epitope
Subtype B
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA, protein, baculovirus *Strain:* B clade IIIB *HIV component:* gp160, Nef, Rev, Tat *Adjuvant:* aluminum phosphate
Species (MHC) human
Country Sweden.
Assay type proliferation, CD8 T-cell Elispot - IFNγ
Keywords HAART, ART, inter-clade comparisons, supervised treatment interruptions (STI), immunotherapy
References Boström *et al.* 2004

- In this study, HIV-infected patients who had previously been immunized with DNA plasmid (nef, tat and ref) or recombinant gp160 were followed longitudinally to determine the impact of HAART on specific T-cell responses. While therapeutic immunizations had transient effects on CD4 cell counts, there was increased survival at 2 years.
- After gp160 vaccination, gp160-specific proliferative CD4+ T cell responses to both baculovirus (MGS HIV-1 rgp 160) and to IMMUNO AG derived gp160 were increased, as well as to p24. Long term HAART treatment was associated with increased IFNγ producing T-cells.
- T-cell proliferative responses to gp160 vaccination were maintained for up to 7 years.

HXB2 Location Env
Author Location Env (HXB2. BaL)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade 1007 *HIV component:* Env, Gag-Pol, Nef
Species (MHC) macaque
Assay type CD4 T-cell Elispot - IFNγ, T-cell Elispot
Keywords variant cross-recognition or cross-neutralization, co-receptor

References Letvin *et al.* 2004

- SIVmac239 gag-pol-nef vaccination of macaques confers better protective responses against a SHIV 89.6 challenge if Env is included even when the vaccine and challenge strain were heterologous in Env. This protection, realized by decreased viral replication and higher levels of CD4+ T cells over time, was associated with T-cell responses early in infection, but not neutralizing Abs.
- The 24 Indian-origin rhesus macaques included in this study did not express Mamu-A*01.

HXB2 Location Env
Author Location
Epitope
Subtype CRF02_AG
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human
Country Senegal.
Assay type CD4 T-cell Elispot - IFNγ
Keywords rate of progression, variant cross-recognition or cross-neutralization
References Zheng *et al.* 2004

- Gag, Env, Tat, and Nef-specific T-cell responses were evaluated in 68 HIV-1 and 55 HIV-2 infected drug naive, generally asymptomatic, infected Senegalese patients.
- HIV-1 peptides were derived from HIV-1 CRF-02 (HIV-1 A/G, AJ251056)and HIV-2 peptides spanning HIV-2 ROD (M15390).
- Gag specific responses dominated in both groups, but overall magnitude and frequencies did not correlate with viral load or CD4 counts. More Nef responses were found in HIV-1 infected people than HIV-2, and Nef in HIV-2 is more diverse.

HXB2 Location Env
Author Location gp120
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol *Adjuvant:* IFNγ, IL-2, IL-4
Species (MHC) mouse (H-2^d)
Keywords Th1
References Kim *et al.* 2000

- Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of Th1 cytokine IFNγ drove Th1 immune responses and enhanced CTL responses.

HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (MHC) mouse (H-2^d)
Keywords Th1, Th2
References Shirai *et al.* 2001

- Helicobacter pylori induces Th1 responses early, but predominantly Th2 responses later in infection (at 6 weeks) – differentiation of HIV-1 gp160 CD4+ help and CD8+ CTL effector cells in response to HIV gp160-vaccinia vaccination is impaired in BALB/c mice infected with H. pylori.

HXB2 Location Env
Author Location gp120 (V3) and p24 (IIIB, MN, BH10)
Epitope
Subtype A, B
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* A clade UG5.94UG018, B clade IIIB *HIV component:* Gag, gp120
Species (MHC) mouse (H-2^d)
Keywords inter-clade comparisons
References Buonaguro *et al.* 2002

- Different HIV strains were used for different regions: gp120 A clade UG5.94UG018; Gag HIV-1 IIIB
- BALB/c mice were given intraperitoneal immunization in the absence of adjuvants with virus-like particles (VLPs) expressing recombinant subtype A gp120 and Pr55gag.
- High dose-independent humoral responses were elicited against both gp120 and p24 peptides, and CTL responses were observed against target cells carrying vaccinia expressed gp120 and Gag.
- Recombinant rgp120 (clade B, MN) induced T cell proliferative responses *in vitro* from vaccinated animals.

HXB2 Location Env
Author Location gp160 (IIIB)
Epitope
Immunogen Vaccine
Vector/Type: peptide, protein *Strain:* B clade IIIB *HIV component:* gp160, V3 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Species (MHC) mouse (H2^d)
Keywords Th1, Th2
References Morris *et al.* 2000

- Mice were intranasally immunized with 20 ug of HIV-gp160 and 5 ug of peptide E7 (RIHIGPGRAFYAARK) with the adjuvant LT(R192G), a heat-labile enterotoxin produced by E. coli.
- Adjuvant LT(R192G) was required for stimulation of antigen-specific IgG1, IgG2 antibodies, and Th1 and Th2 cytokines responses to gp160, and peptide-specific CTL responses.
- Increased IFNγ, IL-10 and IL-6 cytokine production specific to gp160 was measured with co-immunization of gp160 with LT(R192G)

HXB2 Location Env
Author Location gp160 (IIIB)
Epitope
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* Br-cAMP
Species (MHC) mouse (H2^d)
Keywords Th1

References Arai *et al.* 2000

- The CMV promotor responds to the intracellular level of cAMP, and 8 Br-cAMP can increase transgene expression so it was co-administered with a CMV-based DNA vaccine both intranasally and intramuscularly.
- 8 Br-cAMP increased serum IgG responses, HIV-specific CTL, DTH and Th1 responses, and IgA in the intranasal vaccination.
- A CAT assay study showed adjuvant effect was due to CMV promotor activation.

III-B-16 Nef Helper, CD4+, T-cell epitopes

HXB2 Location Nef (1–20)
Author Location Nef (1–20 LAI)
Epitope MGGKWSKSSVVGWPTVRERM
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (1–20)
Author Location Nef (1–20 HXB2)
Epitope MGGKWSKSSVIGWPTVRERM
Subtype B
Immunogen HIV-1 infection
Species (MHC) (H-2^d)
Keywords class I down-regulation by Nef
References Peng & Robert-Guroff 2001

- Deletion of the 19 N-terminal amino acids from Nef including the myristolation signal eliminates Nef-induced down-regulation of MHC class I and CD4 molecules. Such a construct has the potential to serve as a more potent immunogen. The known T-cell epitopes that that would be disputed by this deletion are minimal, a murine H-2d Th epitope in the peptide MGGKWSKSSVIGWPTVRERM, and a HLA-B8 CTL epitope, WPTVRERM.

HXB2 Location Nef (14–22)
Author Location Nef (14–22 SF2)
Epitope SAIRERMRR
Epitope name 95.12, 33.6
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DRw6)
Donor MHC DRw52, DRw6, DRw15(2), DQw1, DQw6, DP4
Assay type proliferation
Keywords epitope processing
References Wentworth & Steimer 1994

- Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity.
- These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.
- The two clones that recognized the epitope SAIRERMRR could also auto-present Nef protein, suggesting that they recognized this epitope in the context of the intact, unprocessed protein.

HXB2 Location Nef (16–35)
Author Location Nef (16–35 LAI)
Epitope VRERMRRAEPAADGVGAASR
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (31–50)
Author Location Nef (31–50 LAI)
Epitope GAASRDLEKHGAITSSNTAA
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (43–49)
Author Location Nef (47–53 SF2)
Epitope ITSSNTA
Epitope name 1.13
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DQw7)
Donor MHC DR1, DR8, DRw52, DQw1, DQw7, DP4
Assay type proliferation
Keywords epitope processing
References Wentworth & Steimer 1994

- Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity.
- These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.

HXB2 Location Nef (45–69)

Author Location Nef (45–69 BRU)
Epitope SSNTAATNAACAWLEAQEEEEVGFP
Immunogen Vaccine
Vector/Type: peptide prime with protein boost *Strain:* B clade BRU *HIV component:* Nef
Species (MHC) chimpanzee, rat
References Estaquier *et al.* 1992

- Antigenic domain: ATNAACAWL, priming with peptide enhanced subsequent Ab response to Nef protein immunization.

HXB2 Location Nef (45–69)
Author Location Nef (45–69)
Epitope SSNTAATNAACAWLEAQEEEEVGFP
Immunogen Vaccine
Vector/Type: peptide *Adjuvant:* aluminum hydroxide
Species (MHC) rat
Keywords vaccine-specific epitope characteristics
References Rouaix *et al.* 1994

- Covalently linking the potent Th epitope Nef 45-69, which can induce Th proliferative responses at low doses with no adjuvant in Lou/M rats, to a weaker epitope from Schistosoma mansoni allows the induction of detectable Th responses to the Schistosoma epitope.

HXB2 Location Nef (46–65)
Author Location Nef (46–65 LAI)
Epitope SNTAATNAACAWLEAQEEEE
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (56–68)
Author Location Nef (56–68 HXB2)
Epitope AWLEAQEEEEVGF
Immunogen Vaccine
Vector/Type: peptide *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse (DQ2, DQ3, DQ5, DQ6, DQ7, DQ8,)
Keywords binding affinity, cross-presentation by different HLA, Th1, TCR usage
References Pancré *et al.* 2002

- This highly conserved Nef epitope has promiscuous HLA-DQ class II binding potential. It has a can bind to 6 different HLA-DQ alleles, but did not bind to any HLA-DR alleles tested. It bound to DQ2 and DQ8 with particularly high affinity, and with DQ7 with low affinity.
- DQ transgenic mice (in particular DQ8) mounted strong cellular and humoral responses after immunization with this peptide.
- Ex vivo stimulation of CD4+ T-cells from 14 healthy donors (with diverse HLAs) with this peptide presented on autologous DCs resulted in Th1-associated cytokine production. IFNgamma production was stimulated in 7/14 cases, both IFNgamma and IL-2 in 6/14, and just IL-2 in 1/14. No IL-4 or IL-5 production was observed.
- Peptide-specific CD4+ T-cell clones with different HLA presenting molecules demonstrated a preference for TCR Vβ6.1.

HXB2 Location Nef (61–80)
Author Location Nef (61–80 LAI)
Epitope QEEEEVGFPVTPQVPLRPMT
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^b)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (64–73)
Author Location Nef (68–77 SF2)
Epitope EEVGFPVRPQ
Epitope name 59.25
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DRw15(2))
Donor MHC DR1, DRw15(2), DQw1, DP4
Assay type proliferation
Keywords epitope processing
References Wentworth & Steimer 1994

- Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity.
- These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.

HXB2 Location Nef (66–73)
Author Location Nef (70–77 SF2)
Epitope VGFPVRPQ
Epitope name 29.16
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DR1, DRw15(2))
Donor MHC DR1, DRw15(2), DQw1, DP4
Assay type proliferation
Keywords epitope processing
References Wentworth & Steimer 1994

- Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity.
- These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.

HXB2 Location Nef (66–97)
Author Location Nef (66–97 LAI)
Epitope VGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGL
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 5/10 reacted to this Nef peptide.
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual.
- 5/12 tested had an IgG response to this peptide.

HXB2 Location Nef (76–95)
Author Location Nef (76–95 LAI)
Epitope LRPMTYKAAVDLSHFLKEKG
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^b)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (81–97)
Author Location Nef (81–97 B Consensus)
Epitope YKAAVDLSHFLKEKGGL
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location Nef (91–110)
Author Location Nef (91–110 LAI)
Epitope LKEKGGLEGLIHSQRRQDIL
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat
Species (MHC) mouse (H-2^b)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (98–112)
Author Location Nef (98–112 BRU)
Epitope EGLIHSQRRQDILDL
Immunogen Vaccine
Vector/Type: peptide prime with protein boost *Strain:* B clade BRU *HIV component:* Nef
Species (MHC) chimpanzee
References Estaquier *et al.* 1992

- Peptide alone could stimulate monkey T-cells in the absence of carrier protein – required carrier protein in rat.

HXB2 Location Nef (104–121)
Author Location Nef (104–121 B Consensus)
Epitope QKRQDILDLWVYHTQGYF
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.

- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location Nef (104–123)
Author Location Nef (106–125 HXB3)
Epitope QRRQDILDLWIYHTQGYFPD?
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade HXB3
HIV component: Nef
Species (MHC) mouse (H-2^b)
References Sandberg *et al.* 2000

- A strong T helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization.
- Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun.
- Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes.

HXB2 Location Nef (106–125)
Author Location Nef (106–125 LAI)
Epitope RQDILDLWIYHTQGYFPDWQ
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^b)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (112–127)
Author Location Nef (112–127 B Consensus)
Epitope LWVYHTQGYFPDWQNY
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 14% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location Nef (117–147)
Author Location Nef (117–147 LAI)
Epitope TQGYFPDWQNYTPGPGVRYPLTFGWCYKLVP
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 1/10 reacted to this Nef peptide.
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual.
- 10/12 tested had an IgG response to this peptide.

HXB2 Location Nef (121–140)
Author Location Nef (121–140 LAI)
Epitope FPDWQNYTPGPGVRYPLTFG
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^b)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (136–155)
Author Location Nef (136–155 LAI)
Epitope PLTFGWCYKLVPVEPDKVEE
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (151–170)
Author Location Nef (151–170 LAI)
Epitope DKVEEANKGENTSLLHPVSL
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^{d})
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (162–178)
Author Location Nef (162–178 B Consensus)
Epitope NSLLHPMSLHGMDDPEK
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 11% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location Nef (164–183)
Author Location Nef (166–185 HXB3)
Epitope LLHPVSLHGMDDPEREVLEW?
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade HXB3
HIV component: Nef
Species (MHC) mouse (H-2^{b})
References Sandberg *et al.* 2000

- A strong T helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization.
- Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun.
- Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes.

HXB2 Location Nef (166–185)
Author Location Nef (166–185 LAI)
Epitope HPVSLHGMDDPEREVLEWRF
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-$2^{b,\,d}$)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (176–193)
Author Location Nef (176–193 B consensus)
Epitope PEKEVLVWKFDSRLAFHH
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DRB1*0401, DRB1*0701, DRB1*1101, DRB1*1302, DRB1*1501, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 36% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The peptides that were recognzied by the most people were able to bind broadly to multiple HLA-DR molecules. This peptide showed high cross-reactive binding capacity and bound to 7/8 tested HLA-DR molecules.

- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location Nef (179–198)
Author Location Nef (181–205 HXB3)
Epitope EVLEWRFDSRLAFHHVAREL?
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade HXB3
HIV component: Nef
Species (MHC) mouse (H-2^b)
References Sandberg *et al.* 2000

- A strong T helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization.
- Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun.
- Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes.

HXB2 Location Nef (181–188)
Author Location Nef (185–192 SF2)
Epitope LVWRFDSK
Epitope name 6.38
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DP5)
Donor MHC DRw11, DRw52, DQw7, DP5
Assay type proliferation
Keywords epitope processing
References Wentworth & Steimer 1994

- Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity.
- These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.

HXB2 Location Nef (181–205)
Author Location Nef (181–205 LAI)
Epitope LEWRFDSRLAFHHVARELHPEYFKN
Subtype B
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade LAI
HIV component: Nef, Rev, Tat
Species (MHC) mouse (H-2^d)
References Hinkula *et al.* 1997

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.

HXB2 Location Nef (182–205)
Author Location Nef (182–205 LAI)
Epitope EWRFDSRLAFHHVARELHPEYFKN
Subtype B
Immunogen Vaccine
Vector/Type: lipopeptide
Species (MHC) human
References Gahery-Segard *et al.* 2000

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.
- A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 4/10 reacted to this Nef peptide.
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual.
- None of the 12 tested had an IgG response to this peptide.

HXB2 Location Nef (184–199)
Author Location Nef (184–199 B consensus)
Epitope KFDSRLAFHHMARELH
Subtype B
Immunogen HIV-1 infection
Species (MHC) human (DRB1*0101, DRB1*0701, DRB1*1101, DRB1*1501, DRB5*0101)
Country United States.
Assay type CD4 T-cell Elispot - IFNγ
Keywords supervised treatment interruptions (STI), immunodominance
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 25% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The peptides that were recognzied by the most people were able to bind broadly to multiple HLA-DR molecules. This peptide showed high cross-reactive binding capacity and bound to 5/8 tested HLA-DR molecules.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location Nef (185–200)
Author Location Nef (183–198)
Epitope FDSRLAFHHVARELHP
Immunogen HIV-1 infection
Species (MHC) human

References Ranki *et al.* 1997

- T-cell response to this epitope persisted after seroreversion.

HXB2 Location Nef (186–206)
Author Location Nef (p27) (185–205 BRU)
Epitope DSRLAFHHVARELHPEYFKNC
Epitope name PF63
Subtype B
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* gp160, Nef, p17/p24 Gag, p25 Gag *Adjuvant:* muramyl-dipeptide base adjuvant (Syntex)
Species (MHC) chimpanzee
Keywords immunodominance
References Bahraoui *et al.* 1990

- Six chimpanzees were immunized with rec vaccinia viruses (VV) expressing HIV-1 gp160, Gag, and Nef.
- 2/6 chimpanzees showed persistent T-helper proliferative responses against a putative immunodominant epitope located at the C-term end of Nef.

HXB2 Location Nef (190–206)
Author Location Nef (190–206 B Consensus)
Epitope AFHHMARELHPEYYKDC
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Country United States.
Assay type CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining, HLA binding
Keywords supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection
References Kaufmann *et al.* 2004

- CD4 T-cell responses in 36 HIV-1 positive individuals in different stages of disease were mapped by IFNgamma EliSpot using a panel of 410 peptides spanning all HIV proteins, derived from the HIV clade B consensus sequence. Virus specific CD4+ T cell responses (median = 7, range of magnitude = 990) were detected in 30/36 patients.
- This peptide was recognized by 14% of the study group.
- Gag and Nef responses dominated the CD4+ T cell Elispot responses in the study. No correlation between plasma viremia and the frequency or magnitude of HIV-1-specific responses was observed.
- The most HIV-1 specific CD4+ T-cell responses were observed in acutely infected patients with treatment of primary infection who stopped acute-STI after 1-3 treatments, compared to patients continuing with therapy. People with therapy during chronic infection had low responses, higher numbers of responses were seen among untreated people. 2/9 long term non-progressors responded to many peptides, comparable to acute STI.

HXB2 Location Nef (191–199)
Author Location Nef (195–203 SF2)
Epitope FHHMARELH
Epitope name 3.2
Subtype B
Immunogen in vitro stimulation or selection
Species (MHC) human (DR1)
Donor MHC DR1, DR8, DRw52, DQw1, DQw7, DP4
Assay type proliferation
Keywords epitope processing
References Wentworth & Steimer 1994

- Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity.
- These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.

HXB2 Location Nef
Author Location Nef (LAI)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
References da Silva & Hughes 1998

- This study compares the level of variation in Nef CTL epitopes to helper and MAb epitopes from the same region.
- CTL epitopes tend to be more conserved than either helper or MAb epitopes and there are stronger functional constraints in the regions where CTL epitopes cluster.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat
Species (MHC) human
Keywords HAART, ART
References Calarota *et al.* 1999

- 9/9 HIV-1 + subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated.
- The nef DNA immunization induced the highest and most consistent CTLp activity, IFNγ production, and IL-6 and IgG responses.
- Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS)
Species (MHC) human
Keywords review, Th1
References Calarota & Wahren 2001

- This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART
References Oxenius *et al.* 2000

- Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords rate of progression, Th1, Th2
References Wilson *et al.* 2000b

- Dysfunction of HIV-1 specific proliferative responses, but not responses to other antigens, is evident in HIV-1 progressive disease.
- Vigorous HIV-1 specific responses to p24, Nef and gp120 with SI between 8-99 were seen in 6/7 long term non-progressors (LTNP), the seventh had a borderline responses. IL-2 production was seen in all cases, and IL-4 production was also evident many responses.
- None of the progressors (0/5) had HIV-1 specific proliferative responses, or IL-2 or IL-4 induction.
- Non-HIV antigens (cytomegalovirus, PPD, Staphylococcus enterotoxin B, tetanus toxoid) gave similar responses in HIV-1 + LTNP, progressors, and HIV-1 controls.

HXB2 Location Nef
Author Location Nef (BRU)
Epitope
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA), PLG
Species (MHC) mouse
Keywords Th2
References Moureau *et al.* 2002

- BALB/c mice were immunized with Nef alone, Nef with Freund's adjuvant, or Nef encapsulated in poly(DL-lactide-co-glycolide) PLG microparticles.
- High Ab titers (predominantly IgG1) against Nef were retained for seven months in the mice infected with Nef-PLG, 3-fold higher than Nef in Freund's, 5-fold higher than Nef alone.
- CD4+ T-cell lymphoproliferative were observed, and cytokine profiles indicated this was primarily a Th2 response.

HXB2 Location Nef
Author Location Nef (SF2)
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Keywords inter-clade comparisons, rate of progression
References Imami *et al.* 2002b

- 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile.
- In a comparison of responses to HIV-1 proteins based on 10 non-progressors, 3 immunologically discordant, and 70 progressors, SIs were always much higher for non-progressors and immunologically discordant than progressors. Among the non-progressors, the responses to different antigens were greater using p24 peptides than native p24. Native p24, Nef, gp120 proteins, and Remune (gp120 depleted HIV-1, p24 is subtype G), had roughly comparable distributions of SI values from the non-progressors, Nef and gp120 responses were somewhat diminished in immunologically discordant patients.

HXB2 Location Nef
Author Location (BRU)
Epitope
Subtype B
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade BRU *HIV component:* RT, virus *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (MHC) mouse
References Haas *et al.* 1991

- Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus.
- B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen
Species (MHC)
References

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC)
Assay type proliferation
Keywords HAART, ART
References Sullivan *et al.* 2003

- Lymphoproliferative responses to HIV antigens p24, gp120 and Nef were enhanced in eight patients who were switched from protease inhibitors to non-nucleoside reverse transcriptase inhibitors.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type cytokine production, proliferation
Keywords HAART, ART
References Hardy *et al.* 2003

- Upon initiating HAART, CD4+ T cell proliferative responses in 36 patients were restored to specific antigens, mitogens, and IL-2. Restored recall responses were largely to persistent antigens, and not to HIV-1 or new antigens, and recall responses were associated with IL-2, not IL-4 production.

HXB2 Location Nef
Author Location Nef
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Nef, Vif, Vpu
Species (MHC) mouse (H-2^d)
Keywords inter-clade comparisons, Th1
References Ayyavoo *et al.* 2000

- Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFNγ levels.
- Antigen stimulation increased IFNγ production in pVVN-P immunized mice, indicating a Th1 response.
- IL-4 production was not significantly changed after antigen stimulation compared to control levels.
- Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.

III-B-17 HIV-1 Helper, CD4+, T-cell epitopes

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords review, HIV exposed persistently seronegative (HEPS), mother-to-infant transmission
References Kuhn *et al.* 2002

- Intrauterine exposure of infants to HIV from their mothers results in HIV-1 specific T-helper cell proliferative responses in 1/3 of exposed uninfected babies, and HIV-1 specific CTL in some. It is unknown whether these responses are associated with lack of infection, but there is some evidence that HIV-1 T-cell responses may reduce transmission in breastfeeding mothers. Summary tables are provided of CD4 and CD8 T-cell responses detected in earlier studies.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human
Keywords HAART, ART, rate of progression
References Kahn *et al.* 2000

- No benefit was observed in terms of progression free survival for HIV-1 patients on ART given vaccinations with HIV-1 antigen (N=1,262) versus those vaccinated with placebo (N=1,265). There was no statistically different outcome in HIV RNA, CD4 percentage, or body weight. HIV-1 ART patients that were vaccinated did have higher absolute CD4 counts.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human
Keywords HAART, ART
References Moss *et al.* 1999

- 15 HIV-1 + patients on ARV given vaccinations with HIV-1 antigen versus vaccinated with placebo. Lymphocyte proliferation of CD4+, CD8+ memory cells and NK cells to p24 and Remune HIV-1 antigen increased in HAART treated patients after vaccination.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human
Keywords Th1
References Moss *et al.* 1997

- HIV-1 specific stimulation of T-cell proliferation, and beta-chemokines (RANTES) and Th1-type cytokine (IFNgamma) production are found after immunization of HIV-1 + individuals with HIV-1 immunogen.

HXB2 Location HIV-1
Author Location

Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human
References Levine *et al.* 1996

- Long-term follow up of HIV-1 + individuals given HIV-1 immunogen, suggesting those patients who became HIV-DTH-responsive in response to the HIV-1 immunogen had a better clinical outcome. Of twelve who developed DTH-responsiveness, one got an opportunistic infection and died, and one developed KS. Of the 13 patients who remained HIV-DTH-nonresponsive, 9 (69%) progressed to AIDS and 7 of these had died.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine
Vector/Type: HIV-1 immunogen *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (MHC) human
References Turner *et al.* 1994

- A dose response study of HIV immunogen in IFA was conducted. Doses of 50, 100, 200, or 400 micrograms (total protein) were tested by DTH skin testing to the inactivated HIV-1 antigen. The HIV-1 immunogen was well tolerated, and the minimum dose required to induce HIV-1 DTH was 100 micrograms.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human, macaque
Keywords dynamics, HAART, ART
References Wodarz 2002

- Mathematical modeling is used to support the idea that T-helper cell dysfunction results in a compromised ability to maintain an anti-HIV CTL memory response. Models suggest strategies to restore CTL memory through therapy and improve long-term immunological control of the virus.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine
Vector/Type: DNA, canarypox, gp120 depleted virus HZ321 (REMUNE(TM)), protein, virus-like particle (VLP), adenovirus *Adjuvant:* GM-CSF, Growth Hormone, IL-12, IL-2, IL-7, CpG immunostimulatory sequence (ISS), Thymosin α-1
Species (MHC) human
Keywords HAART, ART, review, rate of progression, immunotherapy
References Imami *et al.* 2002a

- This review addresses the use of immunotherapy and therapeutic immunization to help chronically infected patients maintain a strong anti-HIV-1 T-cell response. The loss of anti HIV-1 proliferative responses early after infection is reviewed, as are therapeutic vaccinations, with or without HAART, and strategies for immunomodulation that can be given with or without vaccination.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords review, rate of progression, Th1, Th2
References Heeney 2002

- Review of the importance of balanced Th1 and Th2 HIV-specific CD4 T-cell responses in control of infection and for vaccination strategies.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC)
Keywords dynamics, rate of progression, escape
References Bernaschi & Castiglione 2002

- A cellular automata model was used to model the dynamics of HIV-1 infection and progression to disease. The model suggests the long aymptomatic period is due to immune escape mutants with lower viral fitness, and with AIDS resulting from a drastic reduction of the T-helper cell reservoire.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC)
Keywords dynamics, kinetics
References Altes *et al.* 2002

- This study employs a mathematical model to study the consequences of increasing the T-helper response through a vaccine, which would have counter-balancing effects in a new infection: a more intense response provides more help but also more target cells. The model indicates that if the infecting virus had a low replication rate, then CTLp and CD4 helper cells could control an infection. Only a vaccine that could increase CTL responsiveness could reduce viral set point with observed replication rates.
- A CD4+ T-cell response without maintained CTL response was deleterious in this model.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC)
Keywords dynamics, HAART, ART, rate of progression
References Bajaria *et al.* 2002

- This paper presents a dynamical model of HIV infection and progression that includes CD4 T-cell naive and memory populations distributed between the peripheral blood and the lymph nodes, as well as the effects of HAART. Increasing viral replication and infectivity and decreasing T-cell immunity had impact on the rate of disease progression in this model.

HXB2 Location HIV-1
Author Location (HZ321)
Epitope
Subtype AG
Immunogen Vaccine
Vector/Type: gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *Adjuvant:* Incomplete Freund's Adjuvant (IFA), CpG immunostimulatory sequence (ISS)
Species (MHC) mouse
Keywords Th1, Th2
References Ayash-Rashkovsky *et al.* 2002

- Parasitic helminthic infections in humans, common in parts of Africa and Asia, can shift immune responses to Th2 responses. To model this, BALB/c mice were infected with the parasite Schistosoma mansoni, and the infected mice showed a dominant Th2 immune response. Vaccination with gp120-depleted HIV-1 viral particles and incomplete Freund's adjuvant induced Th2 responses in these mice, but this could be shifted towards a Th1 profile when CpG oligodeoxynucleotide was added to the vaccine as an immunostimulatory agent.

HXB2 Location HIV-1
Author Location HIV-1 except gp120
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, rate of progression
References Ghanekar *et al.* 2001

- 12 long term non-progressors (>10 years) went on HAART, while 14 elected not to go on HAART. After a year on HAART, higher frequencies and absolute numbers of HIV-specific memory CD4+ T-cells were observed in untreated patients than patients receiving HAART therapy, tested by stimulation an proliferation responses to HIV Remune antigen (gp120 depleted vaccine).
- These results indicate a control of viral replication in therapy-naive patients may be mediated by their ability to respond to recall viral antigen, and that the diminished response in treated patients may contribute to viral rebound.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords HAART, ART, Th2
References Pido-Lopez *et al.* 2002

- The thymic output in HAART-treated HIV-1 infected patients with progressive disease was studied. One patient also receiving steroid treatment therapy had a weak response in a sjTREC assay indicating a dysfunctional thymus, while four patients not on steroids had clear positive sjTREC readings after HAART. Stimulation of PBMC with multiple recall antigens including gp120, p24 and Nef and mitogens, and revealed that in the patient treated with steroids there was and induction of a Th2 type response indicated by increased levels of IL-4 secretion in response to antigen.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine
Vector/Type: peptide *Adjuvant:* GM-CSF, IL-12, IL-2, IL-4, Tumor Necrosis Factor α (TNFα)
Species (MHC)
Assay type Th support of CTL response
Keywords binding affinity, review, Th1, Th2, mucosal immunity
References Berzofsky 2001

- Vaccine clusters were constructed containing T helper, CTL aand neutralizing antibody epitopes, and used to immunize mice. Four things were found to enhance the vaccine immune response: i) increasing the affinity of the peptide for the presenting MHC molecule, called epitope enhancement; ii) increasing the avidity of MHC/peptide complex for the T-cell receptor; iii) incorporating cytokines IL-2, GM-CSF, TFN-α, or IL-12 and IL-4 which steer responses towards Th1 or Th2 responses; iv) inducing mucosal immunity specifically, with intrarectal being most effective.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag *Adjuvant:* B7, GM-CSF, IL-12, IL-15
Species (MHC) human
Keywords review, Th1, Th2
References Boyer *et al.* 2002

- The first generation of HIV-1 plasmid vaccines in 167 individuals induced T-helper responses in most vaccine recipients, however CTL responses were below a 20% response rate. REV-independent RNA optimized constructs (pGag and pEnv) as well as B7 costimulatory molecules could significantly enhance CD8 effector cell responses. Co-administered GM-CSF enhanced antibody repsonses, IL-12 CTL production. IL-15 increased T cell expansion without increasing T cell help.

HXB2 Location HIV-1
Author Location HIV-1
Epitope
Immunogen HIV-1 infection
Species (MHC)
Assay type cytokine production
Keywords review
References Breen 2002

- HIV-1 triggers immunological dysfunction in multiple ways, including the loss of CD4-positive T helper cells in quantity and function and hyperactivity and changes in the production and activity of cytokines. The role of pro- and anti-inflamatory cytokines are discussed, including IL-10, which can suppress HIV-1, and IL-1, IL-6, TNFα which up-regulate HIV-1.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Assay type cytokine production, proliferation
References Clerici *et al.* 1993b

- rCD4-IgG treatment was associated with improved Th cell function measured by IL-2 production in response to alloantigen or PHA, but not to influenza (a recall antigen response), in 9/10 patients. No clinical benefit was evident. rCD40IgG was also shown to block gp120 induced suppression of Th cells *in vitro*. Proposed mechanisms include: inhibiting HIV-cell fusion by blocking the binding of gp120 to CD4, competing with free gp120 for binding to the CD4 receptor and reducing gp120 induced immunosupression, and gp120-induced direct killing of Th cells.

HXB2 Location HIV-1
Author Location Nef
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords assay standardization/improvement
References Draenert *et al.* 2003

- Six different HIV-1 Nef peptide sets ranging in length from 15-20 amino acids with overlap from 10-11 amino acids derived from either the B clade consensus sequences or the B clade sequence B.AU.AF064676 were used to study the impact of using different peptide design strategies to detect CD4 and CD8 T-cell responses. 20 individuals were tested using the six sets of peptides. 17/20 had CD8 T-cell responses to all peptides sets, and 15 of these 17 had CD4 T-cell responses.

HXB2 Location HIV-1
Author Location Nef
Epitope
Subtype B
Immunogen HIV-1 infection
Species (MHC) human
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining
Keywords assay standardization/improvement
References Draenert *et al.* 2003

- Six different HIV-1 Nef peptide sets ranging in length from 15-20 amino acids with overlap from 10-11 amino acids derived from either the B clade consensus sequences or the B clade sequence B.AU.AF064676 were used to study the impact of using different peptide design strategies to detect CD4 and CD8 T-cell responses. 20 individuals were tested using the six sets of peptides. 17/20 had CD8 T-cell responses to all peptides sets, and 15 of these 17 had CD4 T-cell responses.
- Although there was a trend in detecting more CD8 T cell responses using the shorter 15-mer peptides, longer 20-mers were best for detecting more CD4 T-cell responses, but neither result was statistically significant. Similar results were seen in the 15 to 20 amino acid range for both IFN gamma Elispot and ICS assays.
- Use of the consensus versus the natural strain identified slightly increased numbers of reactive peptides. Seven reactive peptides were observed with the B consensus peptides but not the B.AU.AF064676 peptides, but on the other hand four reactivites were observed using the B.AU.AF064676 peptides but not the consensus.
- Using an overlap of 10 or 11 amino acids did not make a difference.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC)
Assay type cytokine production
Keywords HAART, ART
References Galli *et al.* 2003

- HIV-1-infected women who developed Adepose tissue alterations (ATA) while recieving antiretroviral treatment (ART) had a favorable immunological profile with efficient IL-2 production and T-helper function. The authors suggest that ATA may be related to the ART-driven restoration of immune function.
- The most prominant feature of women with ATA that were recieving ART was increased IL-12 production with a lower TNF alpha and IL-10 synthesis.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC)
Keywords review
References Norris & Rosenberg 2002

- This paper reviews the role of Th cells in controlling HIV-1 infection, and in other viral infections. It describes CD4+ T-cell support of Ab production, CTL responses, as well as antiviral cytokine production and infected-cell killing. HIV+ patients with a low viral load and rare virgorous HIV-specific CD4+ proliferative responses, and the benefit of early treatment in preserving Th HIV-specific responses allowing immune control when therapy is subsequently stopped, are described.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords review, rate of progression, acute infection
References Norris & Rosenberg 2001

- This review goes over the evidence for HIV-1 specific T-helper cell and CTL responses being critical inhibiting viral replication. LTNPs and those treated during acute HIV-1 infection generate specific T-helper responses, but most chronically infected individuals do not.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 and GBV-C co-infection
Species (MHC) human
Assay type cytokine production
Keywords HAART, ART, rate of progression, Th1, Th2
References Nunnari *et al.* 2003

- HIV-1 positive patients co-infected the GBV-C, the hepatitis G virus, have a longer survival time to AIDs and higher CD4+ T cell counts than patients that were not infected with GBV-C. GBV-C co-infected patients showed an intact Th-1 profile over time, with high serum levels of IL-2 and IL-12, and diminishing Th-2 responses reflected by lower levels of IL-4 and IL-10. The opposite was true for HIV-1 + patients that were not co-infected with GBV-C.
- AIDs progression is slower in patients infected with both HIV-1 and hepatitis G virus. It is unclear whether Th-2 and Th-1 cytokines in co-infected patients show cause or consequence of slower AIDs progression. CD4+ cells may support hepatitis G replication.

HXB2 Location HIV-1
Author Location HIV-1
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Keywords dynamics, acute infection
References Korthals Altes *et al.* 2003

- A model of progression was developed that explicitly assumes CD4+ T-cells are both targets of infection and mediators of the immune response. In this model, high viral inoculum with few initial CD4+ T-cells resulted in target-cell-limited infection and high viral load, but with many CD4+ clones and low initial inoculum, infection was controlled by CD4+ clones.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine
Vector/Type: DNA *Adjuvant:* GM-CSF, IFNγ, IL-12, IL-15, IL-18, IL-1α, IL-2, IL-2/Ig, MIP-1α, Tumor Necrosis Factor α (TNFα), Tumor Necrosis Factor β (TNFβ), M-CSF, G-CSF, IL-8, SDF-1α, RANTES, MCP1
Species (MHC)
Keywords review, Th1, Th2, adjuvant comparison
References Calarota & Weiner 2004

- Review summarizes the developments of DNA vaccine enhancement/modulation by 1) improving Th1 cytokine-encoding plasmids 2) by prime-boost vaccine regimens and 3) by chemokine- or T -cell costimulatroy molecule encoding plasmids. Studies involving many approaches for stimulating Th1 responses upon vaccination are compared, and given the initial promise of these strategies, future studies of coadministration or prime boosting with different combinations are advocated.

HXB2 Location HIV-1
Author Location p24 (HIV-2 ROD, HIV-1 IIIB)
Epitope
Immunogen HIV-1 or HIV-2 infection
Species (MHC) human
Country Gambia.
Assay type cytokine production, proliferation, CD8 T-cell Elispot - IFNγ, Chromium-release assay
Keywords rate of progression
References Jaye *et al.* 2004

- A comparison of T cell responses in HIV-1 and HIV-2 infected asymptomatic patients with CD4+ cell counts of 20% showed no significant difference between both groups. Viral loads were roughly 20 times greater in HIV-1 positive patients than HIV-2 positive patients.
- 10/20 (50%) of HIV-1 infected patients demonstrated proliferative responses with SI greater than 1.4 to gp120, and 11/20 to p24. 8/29 (29%) of HIV-2 infected patients recognized gp105, and 8/29 (29%) p26. Cytokine responses in both groups did not differ.
- 9/21 (43%) of HIV-1 + and 15/30 (50%) of HIV-2 + patients had cyotoxic T cell responses to Gag, and 3/21 (14%) HIV-1 + and 8/30 (27%) HIV-2 + responded to Pol.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection
Species (MHC) human
Country Spain.
Assay type proliferation, Intracellular cytokine staining
Keywords HAART, ART
References López *et al.* 2004

- A clinical trial compared chronically HIV-1 infected patients who had replaced HAART with didanosine (ddI) and hyroxyurea (HU) were followed for 12 months to an untreated HIV+ group and a group that continued on HAART.
- Approximately 20% of the patients treated with ddI-HU had detectable CD4+ T-cell proliferative responses to Gag and Env in contrast to drug-naive and HAART treated HIV-infected patients, who had few or no responses.
- HIV-specific CD8+ T-cell responses were higher in ddI-HU treated patients than HAART treated patients, even in individuals that maintained undetectable viral loads.

HXB2 Location HIV-1
Author Location Tat (89.6)
Epitope
Immunogen Vaccine
Vector/Type: DNA prime with protein boost, ISCOM *Strain:* B clade IIIB, SIV *HIV component:* Env, Gag, Tat *Adjuvant:* Immune stimulating complexes (ISCOM)
Species (MHC) macaque
Assay type cytokine production, proliferation, CD8 T-cell Elispot - IFNγ

Keywords vaccine-specific epitope characteristics, Th1, Th2, vaccine antigen design
References Mooij *et al.* 2004

- This study compared vaccinating with Tat alone to vaccinating with Tat+Gag+Env. Rhesus macaques (Macaca mulatta) were intramuscularly immunized with a combination of DNA plasmids (HIV-1 IIIB expressing Tat, SHIV-1 89.6P expressing gp120 and SIV mac239 expressing Gag, followed by three boosts with HIV-1 Tat (IIIB) and Env (89.6, gp140) SIV Gag protein. Animals with multi-antigen vaccination had reduced viremia increased CD4+ T-cell counts.
- Tat-Env-Gag immunized animals had weaker Tat-specific Th responses in comparison to animals immunized with Tat alone; but the response to Tat alone was a Th2 response that did not protect from challenge.
- Immunization with Tat-Env-Gag boosted proliferation of Gag-specific IFN-γ and IL-2 producing cells in 3/4 animals (Th1 and Th2 responses) and induced a Th2-immune response (IL-2, IL-4) to Env.
- CD4+ T helper responses to Tat-Env-Gag immunization were correlated with control and reduction of viremia, suggesting a combination of Th1 and Th2 vaccine responses to multiple HIV antigens is advantageous.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen Vaccine

Species (MHC) macaque
Keywords review
References Heeney 2004

- Review discusses the status, design and selection of novel HIV vaccines which elicit strong T-helper responses which can in turn can elicit CTL and Ab responses.
- Review discusses the status, design and selection of novel HIV vaccines which elicit strong T-helper responses which can in turn can elicit CTL and Ab responses.

HXB2 Location HIV-1
Author Location
Epitope
Immunogen HIV-1 infection, Vaccine

Species (MHC) human
Keywords review, immunotherapy, adjuvant comparison
References Wahren & Liu 2004

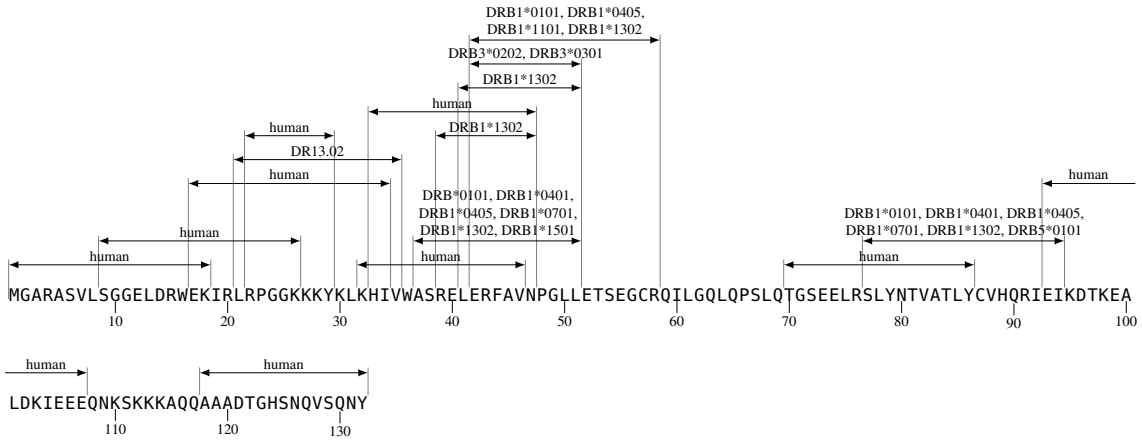
- This review covers immunotherapeutic vaccines use in combination with antiretrovial therapy and use of vaccination in combination with adjuvants and immunomodulators.

III-C

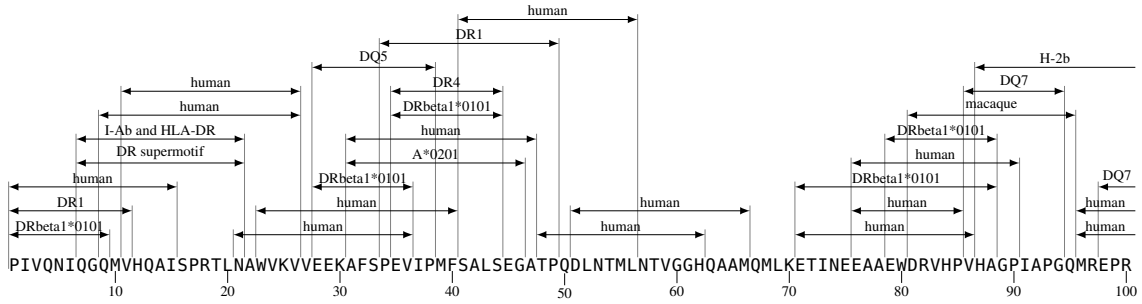
Maps of T-Helper Epitope Locations Plotted by Protein

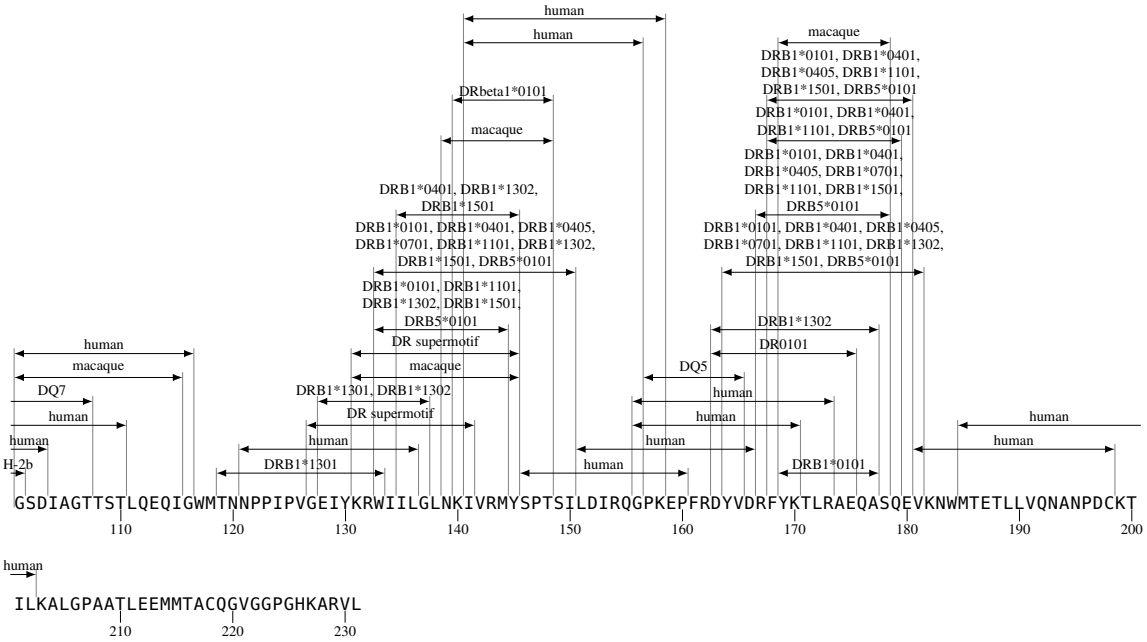
Linear helper T cell epitopes mapped to within a region of 18 amino acids or less are shown.

III-C-1 Gag p17 T-Helper, CD4+, Epitope Map

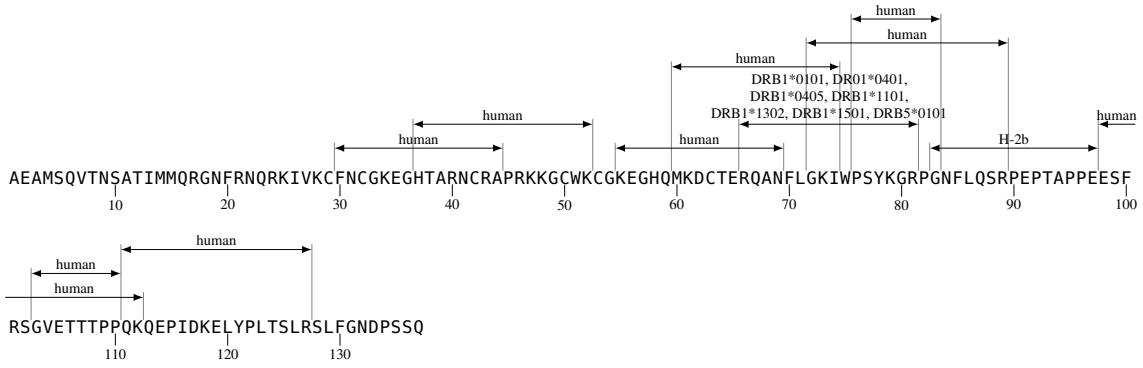


III-C-2 Gag p24 T-Helper, CD4+, Epitope Map



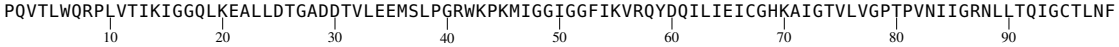


III-C-3 Gag p2p7p1p6 T-Helper, CD4+, Epitope Map

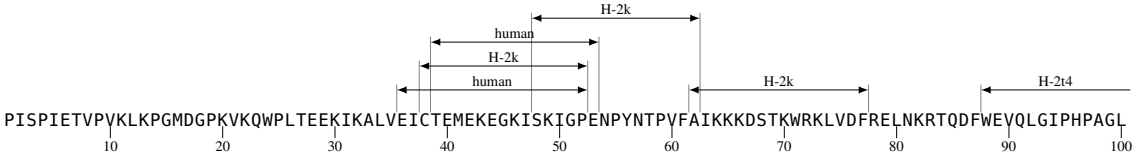


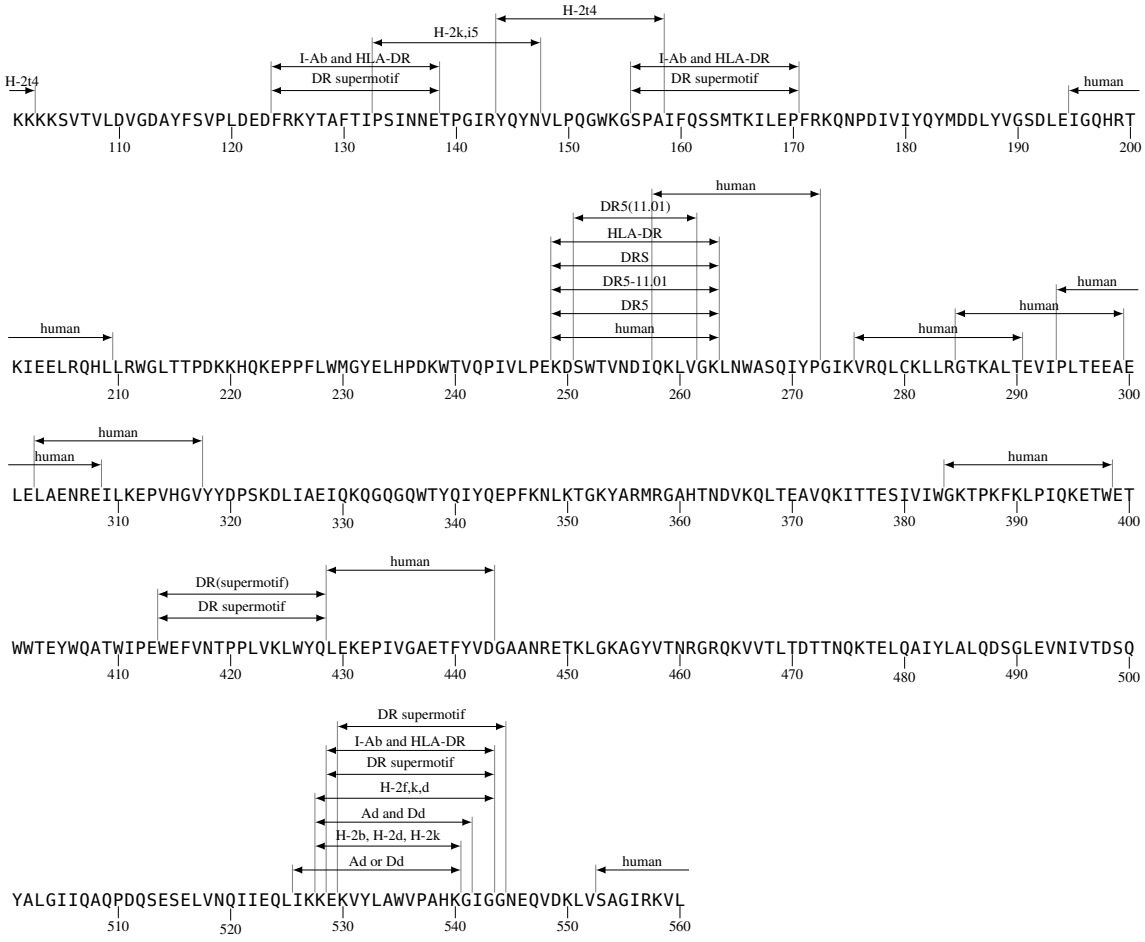
III-C-4 Gag/Pol TF T-Helper, CD4+, Epitope Map

III-C-5 Protease T-Helper, CD4+, Epitope Map

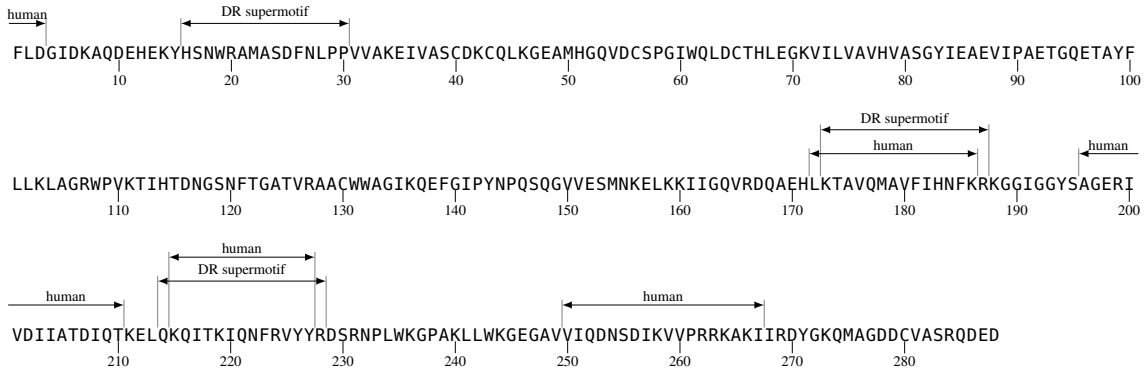


III-C-6 RT T-Helper, CD4+, Epitope Map

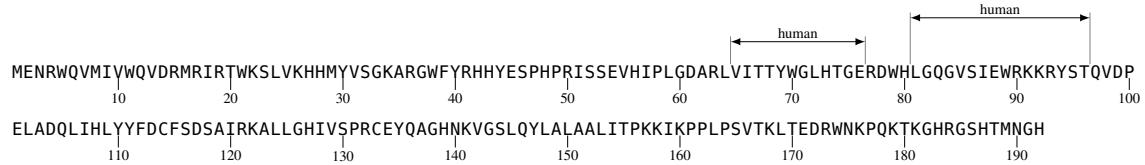




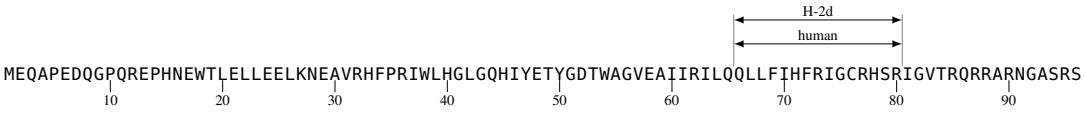
III-C-7 Integrase T-Helper, CD4+, Epitope Map



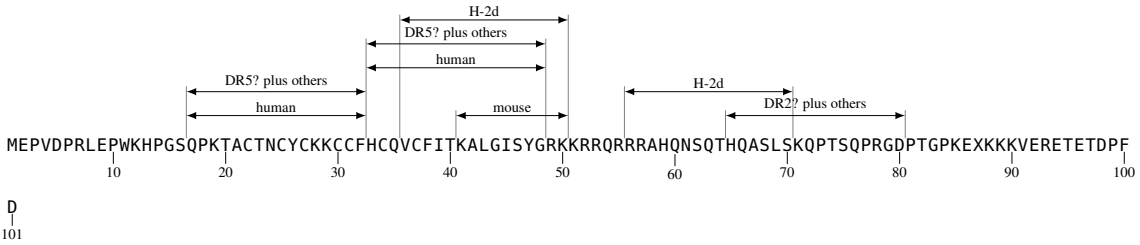
III-C-8 Vif T-Helper, CD4+, Epitope Map



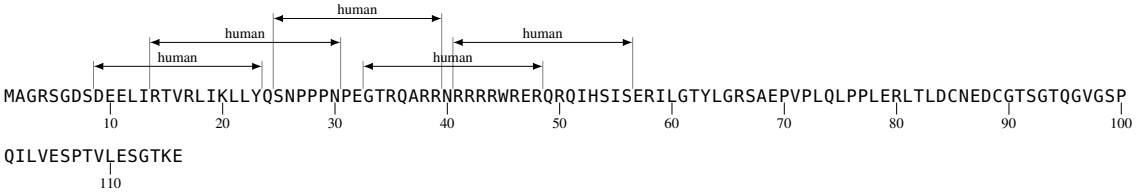
III-C-9 Vpr T-Helper, CD4+, Epitope Map



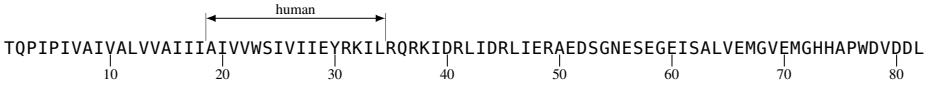
III-C-10 Tat T-Helper, CD4+, Epitope Map



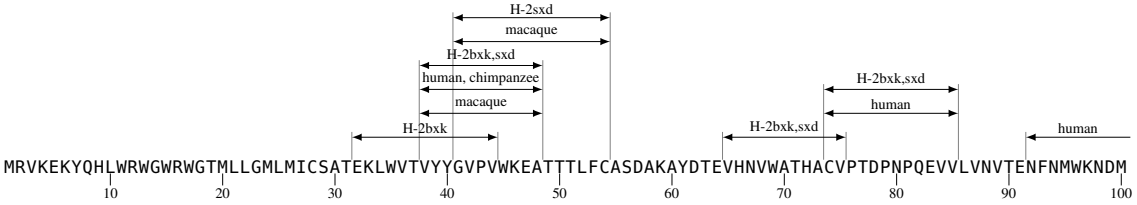
III-C-11 Rev T-Helper, CD4+, Epitope Map

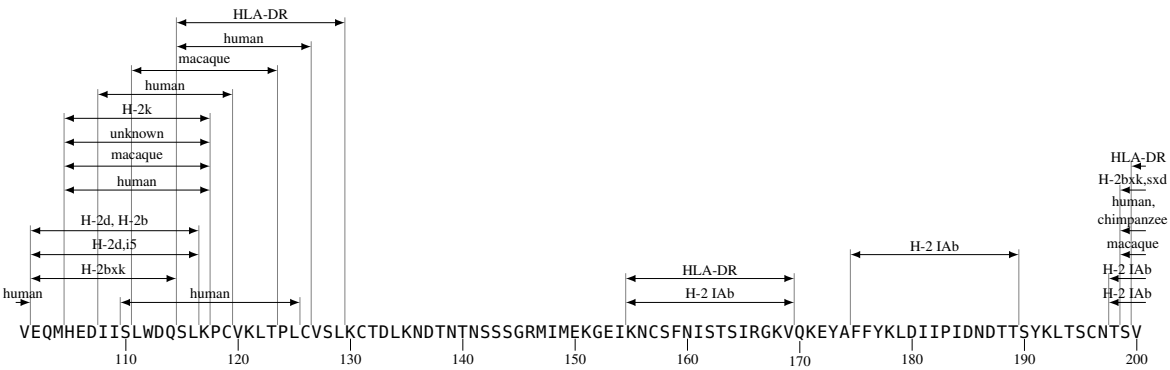


III-C-12 Vpu T-Helper, CD4+, Epitope Map



III-C-13 gp160 T-Helper, CD4+, Epitope Map

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macaque
human
H-2k
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human
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H-2d,i5
H-2bxk
human
human
HLA-DR
H-2 IAb
H-2 IAb
HLA-DR
H-2bxk,sxd
human,
chimpanzee
macaque
H-2 IAb
H-2 IAb
VEQMHEDIISLWDQSLKPCVKLTPLCVSLKCTDLKNDTNTNSSSGRMIMEKGEIKNCSFNISTSIRGKVQKEYAFFYKLDIIPIDNDTTSYKLTSCNTSV
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120
130
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150
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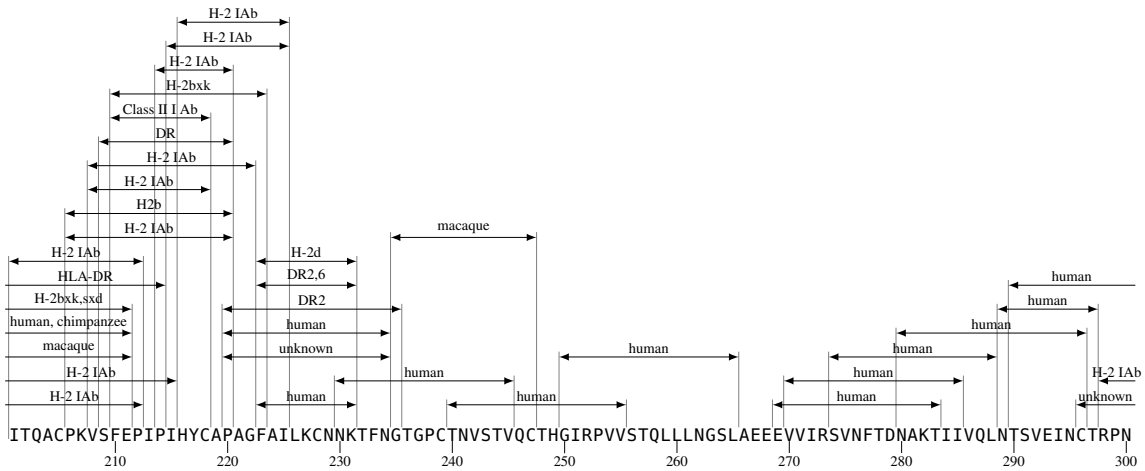
170
180
190
200


H-2 IAb
H-2 IAb
H-2 IAb
H-2bxk
Class II I Ab
DR
H-2 IAb
H-2 IAb
H2b
H-2 IAb
macaque
H-2 IAb
HLA-DR
H-2bxk,sxd
human, chimpanzee
macaque
H-2 IAb
H-2 IAb
H-2d
DR2,6
DR2
human
unknown
human
human
human
human
human
human
human
human
human
H-2 IAb
unknown
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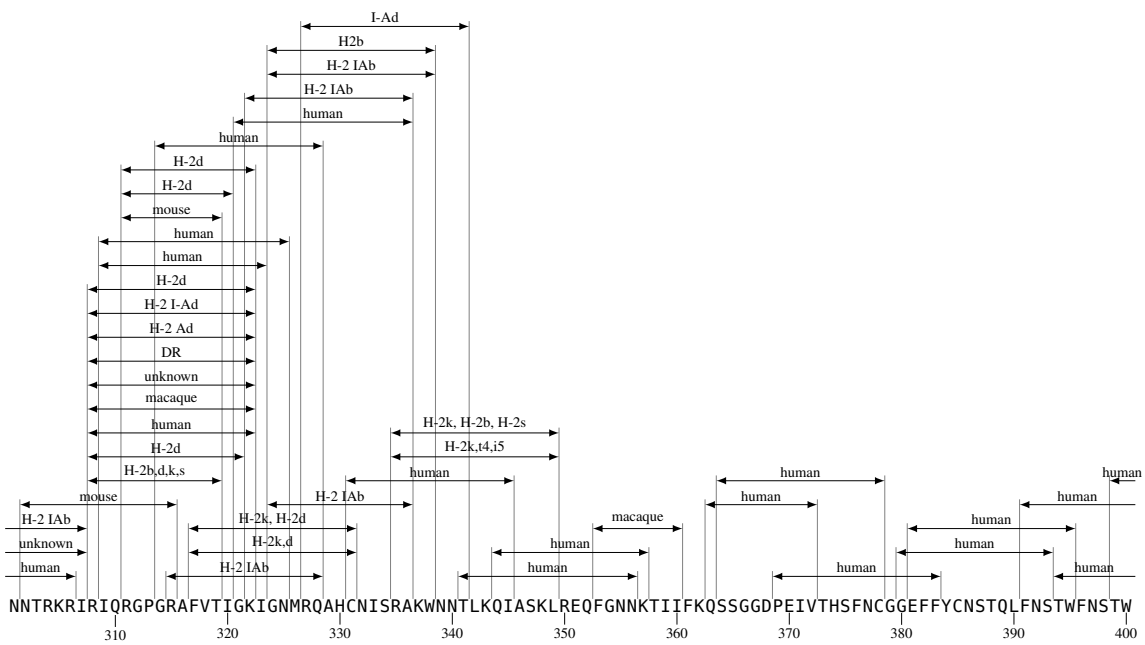
I-Ad
H2b
H-2 IAb
H-2 IAb
human
human
H-2d
H-2d
mouse
human
human
H-2d
H-2 I-Ad
H-2 Ad
DR
unknown
macaque
human
H-2d
H-2b,d,k,s
H-2k, H-2b, H-2s
H-2k,t4,i5
human
mouse
H-2 IAb
H-2 IAb
H-2k, H-2d
H-2k,d
unknown
human
H-2 IAb
macaque
human
human
human
human
human
human
human
human
human
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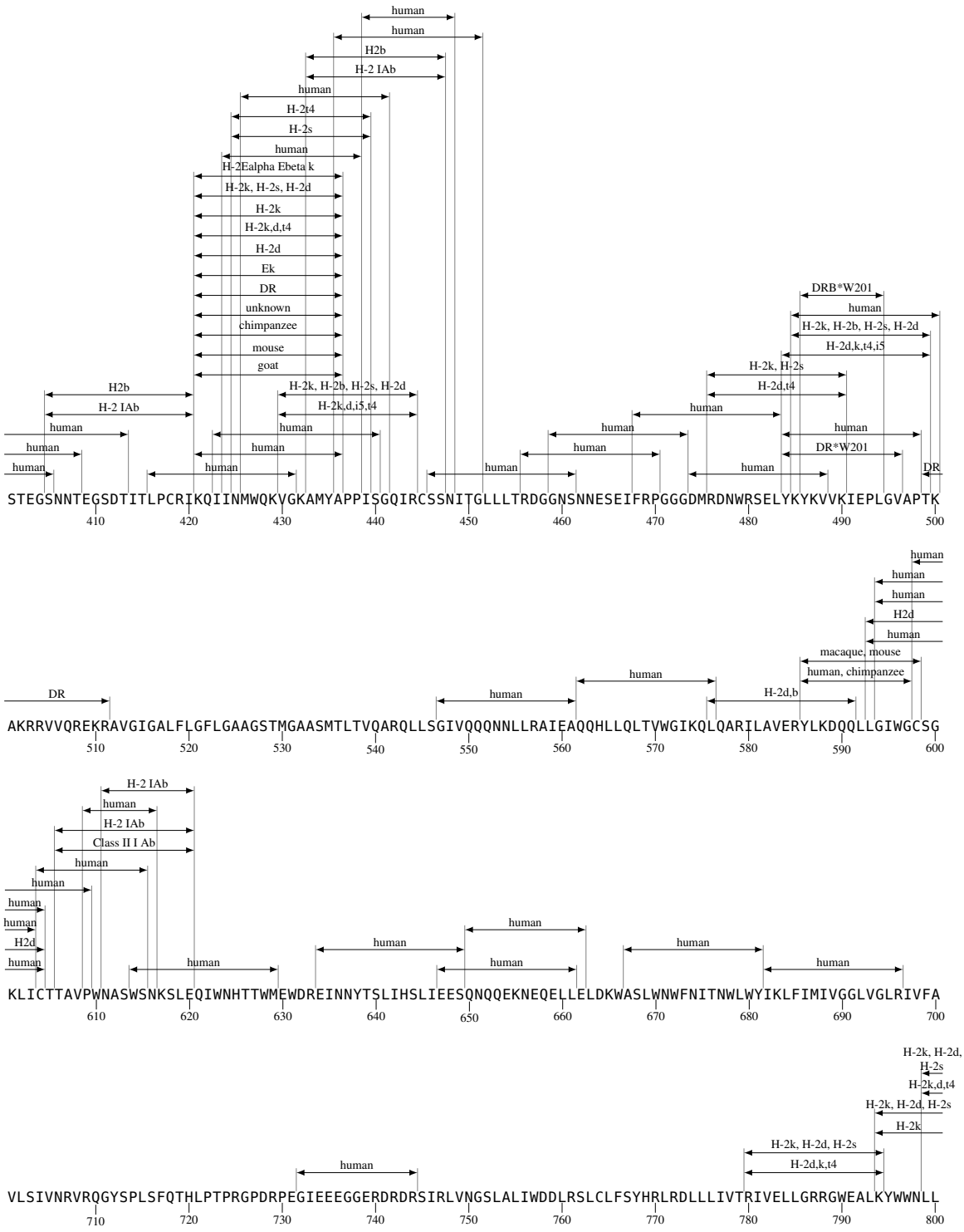
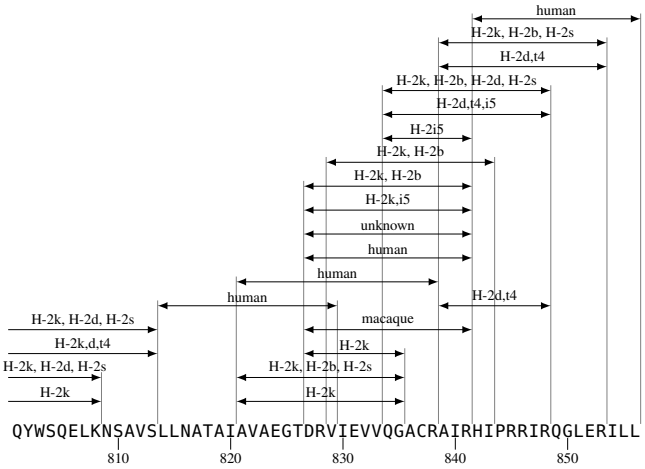
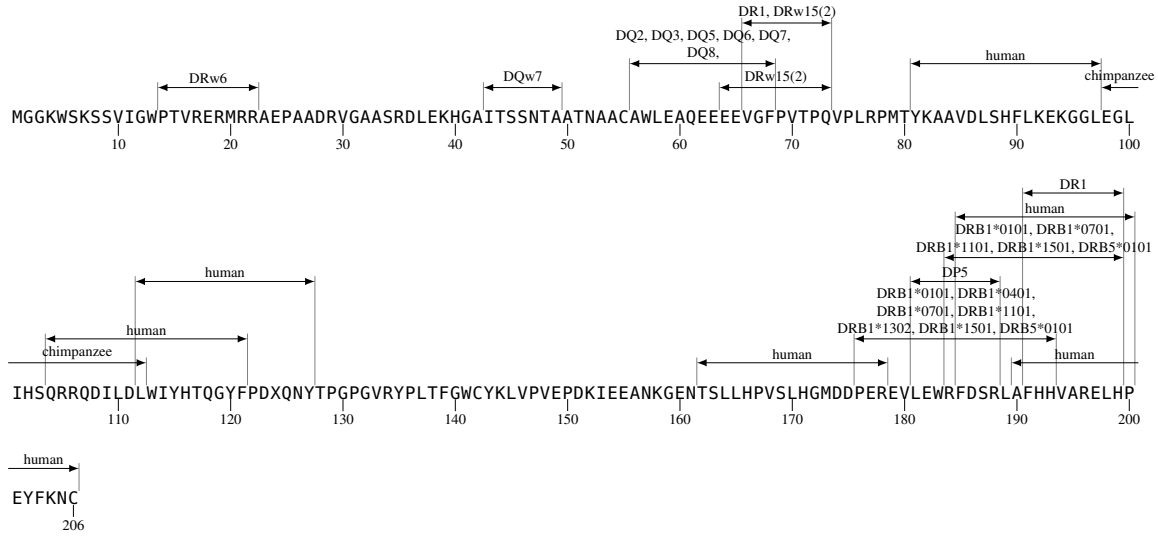
310
320
330
340
350
360
370
380
390
400

T-Helper CD4+


human
human
H2b
H-2 IAb
human
H-2t4
H-2s
human
H-2Ealpha Ebeta k
H-2k, H-2s, H-2d
H-2k
H-2k,d,t4
H-2d
Ek
DR
unknown
chimpanzee
mouse
goat
DRB*W201
human
H-2k, H-2b, H-2s, H-2d
H-2d,k,t4,i5
H-2k, H-2s
H-2d,t4
H2b
H-2 IAb
H-2k, H-2b, H-2s, H-2d
H-2k,d,i5,t4
human
human
human
human
human
human
human
human
human
human
human
DR*W201
DR
STEGSNNTEGSDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNITGLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTK
410 420 430 440 450 460 470 480 490 500
human
human
human
H2d
human
macaque, mouse
human, chimpanzee
human
DR
human
H-2d,b
AKRRVVQREKRAVGIGALFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
510 520 530 540 550 560 570 580 590 600
H-2 IAb
human
H-2 IAb
Class II I Ab
human
human
human
H2d
human
human
human
human
human
human
human
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWFNITNWLWYIKLFIMIVGGLVGLRIVFA
610 620 630 640 650 660 670 680 690 700
H-2k, H-2d, H-2s
H-2k,d,t4
H-2k, H-2d, H-2s
H-2k
H-2k, H-2d, H-2s
human
H-2d,k,t4
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVNGSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
710 720 730 740 750 760 770 780 790 800



III-C-14 Nef T-Helper, CD4+, Epitope Map



Part IV

HIV Antibody Binding Sites

IV-A

Summary

Part IV summarizes HIV-specific antibodies (Abs) arranged sequentially according to the location of their binding domain, organized by protein. We attempted to make this part as comprehensive as possible. For the monoclonal antibodies (MAbs) capable of binding to linear peptides, we require that the binding site be contained within a region of 30 or so amino acids to define the epitope, but not that the precise boundaries be defined. MAbs that do not bind to defined linear peptides are grouped by category at the end of each protein. Antibody categories, for example CD4 binding site (CD4BS) antibodies, are also noted in the index at the beginning of this part. Studies of polyclonal Ab responses are also included. Responses that are just characterized by binding to a protein, with no known specific binding site, are listed at the end of each protein. For more recent updates, epitope sequence alignments, and search capabilities, please see our web site: `http://www.hiv.lanl.gov/content/immunology`.

IV-A-1 Indices

Three indices are provided. The first provides a concise list of anti-HIV-1 MAbs by cross-competition category, with both discontinuous epitopes (for example, CD4BS) and some well known linear epitopes (for example, cluster I) summarized. The second lists the MAbs' IDs in alphabetical order so one can find their location in the table. The third is a listing by order of appearance in the tables.

IV-A-2 Tables

Each MAb has a twelve-part basic entry:

Number: Order of appearance in this table.

MAb ID: The name of the monoclonal antibody with synonyms in parentheses. MAbs often have several names. For example, punctuation can be lost and names are often shortened (M-70 in one paper can be M70 in another). Polyclonal responses are listed as "polyclonal" in this field.

HXB2 location: Position of the antibody binding site relative to the viral strain HXB2 (GenBank Accession Number K03455), which is used as a reference strain throughout this publication. The numbering in this table corresponds to the protein maps. Because of HIV-1 variation the epitope may not actually be present in HXB2; rather, the position in HXB2 indicates the position aligned to the epitope. HXB2 was selected as the reference strain because so many studies use HXB2, and because crystal structures for HXB2-related proteins are often available. The precise positions of an epitope on the HXB2 reference strain can be readily obtained using the interactive position locator at our web site: `http://www.hiv.lanl.gov/content/hiv-db/LOCATE/locate.html`.

Author location: The amino acid positions of the epitope boundaries and the reference sequence used to define the epitope are listed as given in the primary publication. Frequently, these positions as published are imprecise, and do not truly correspond to the numbering of the sequence, but they provide a reasonable guide to the peptide's approximate location in the protein. Also, in many cases, position numbers were provided but the reference sequence identification was not. Because of HIV-1's variability, position numbers require a reference strain to be meaningful. Binding sites that cannot be defined through peptide binding or interference studies are labeled as discontinuous. The approximate location on the protein, sequence number, and reference sequence are listed.

Sequence: The amino acid sequence of the binding region of interest, based on the reference strain used in the study defining the binding site. On occasions when only the position numbers and not the actual peptide sequence were specified in the original publication, we tried to fill in the peptide sequence based on the position numbers and reference strain. If the sequences were numbered inaccurately by the primary authors, or if we made a mistake in this process, we may have misrepresented the binding site's amino acid sequence. Because of this uncertainty, epitopes that were not explicitly written in the primary publication, that we determined by looking up the reference strain and the numbered location, are followed by a question mark in the table.

Subtype: The subtype under study, generally not specified for B subtype.

Neutralizing: **L**: neutralizes lab strains. **P**: neutralizes at least some primary isolates. **no**: does not neutralize. No information in this field means that neutralization was either not discussed or unresolved in the primary publications referring to the MAb.

Immunogen: The antigenic stimulus of the original B cell response. Often this is an HIV-1 infection. If a

vaccine was used as the original antigenic stimulation, not a natural infection, this is noted on a separate line, and additional information about the vaccine antigen is provided as available.

Species(Isotype): The host in which the antibody was generated, and the isotype of the antibody.

Research Contact: Information about an antibody or how to obtain it, as well as to provide credit.

Country: The country where the samples were obtained—generally not specified if the study was conducted in the United States.

References: All publications that we could find that refer to the use of a specific monoclonal antibody. First is a list of all references. Additional details for some of the older references can be found in Part V, although we have tried to keep the entries self-contained since 1997. The "donor" field is meant to serve as a potential guide to a source of information about an antibody or how to obtain it, as well as to provide credit.

Keywords: Keywords for antibody entries were initiated in 2004. The set of keywords includes acute infection; ADCC; adjuvant comparison; anti-idiotype; antibody binding site definition and exposure; antibody generation; antibody interactions; antibody sequence, variable domain; assay development; assay standardization; autologous responses; binding affinity; brain/CSF; coreceptor; complement; enhancing activity; escape; genital and mucosal immunity; HAART; HIV exposed persistently seronegative (HEPS); immunodominance; immunoprophylaxis; immunotherapy; immunotoxin; interclade comparisons; isotype switch; kinetics; mimotopes; mother-to-infant transmission; mucosal immunity; rate of progression; responses in children; review; structure; Th1; Th2; vaccine antigen design; vaccine-induced epitopes; vaccine-specific epitope characteristics; and variant cross-recognition or cross-neutralization. The keywords are listed when available as part of the main entry, and also follow the note in bold type so references pertaining to particular types of studies can be found quickly.

Notes: Describe the context of each study, and what was learned about the antibody in the study.

IV-A-3 HIV protein binding site maps

The names of MAbs and the location of well characterized linear binding sites of 21 amino acids or less are indicated relative to the protein sequences of the HXB2 clone. This map is meant to provide the relative location of epitopes on a given protein, but the HXB2 sequence may not actually bind to the MAb of interest, as it may vary relative to the sequence for which the epitope was defined. Above each linear binding site, the MAb name is given followed by the species in parentheses. Human is represented by 'h', non-human primate by 'p', mouse by 'm', and others by 'o'. More precise species designations for any given MAb can be found using the web search interface or in the tables in this part.

IV-A-4 Alignments

To conserve space, no epitope alignments are provided in this book, but they can be generated using the MAb search tool at `http://www.hiv.lanl.gov/content/immunology`. All epitopes are aligned to the HXB2 sequence, with the sequence used to define the epitope indicated directly above it. Sequences are sorted by their subtype and country of origin.

The master alignment files from which the epitope alignments were created are available at our web site[1]. The alignments were modified in some cases to optimize the alignment relative to the defined epitope and minimize insertions and deletions; epitope alignments are generated by anchoring on the C-terminal residue. A dash indicates identity to the consensus sequence, and a period indicates an insertion made to maintain the alignment. Stop codons are indicated with a `$`, and frameshifts by a `#`, or ambiguous codons (nucleotide was `r`, `y`, or `n`) by an `x`; they are inserted to maintain the alignments. In consensus sequences an upper case letter indicates the amino acid was present in all sequences, a lower case letter indicates the amino acid was present in most sequences in a given position, and a question mark indicates two or more amino acids were represented with equal frequency.

[1] `http://www.hiv.lanl.gov/content/hiv-db/ALIGN_CURRENT/ALIGN-INDEX.html`

IV-B

Cross Reference Listing of MAbs

IV-B-1 MAbs by binding type

Cross reference by protein and binding type of MAb names and their order of appearance in the tables.

Binding type	MAb ID (No.)
p17	
C-term	sc-FV p17 (34)
p24	
C-term	13B5 (115)
Protease	
N-term	1696 (173)
flap region	F11.2.32 (175)
RT	
C2	polyclonal (181)
palm domain	6B9 (201)
thumb domain	5F (202), 5G (203), 7C4 (204)
Integrase	
Integrase DNA binding domain	5D9 (221), 2-19 (224), 8-22 (225), 4-20 (226), 6-19 (227)
Integrase catalytic core	7-16 (218), 4F6 (219)
N-term	1C4 (205), 2C11 (206), 2E3 (207), 3E11 (208), 3F9 (209), 5F8 (210), 6G5 (211), 7B6 (212), 7C6 (213), 6C5 (214), 4D6 (217)
Pol	
C-term	33 (252), F-6 (253)
Vif	
C-term	TG001 (255)
Tat	
C-term	polyclonal (259), polyclonal (270), polyclonal (271), 1D2F11 (273), 2D9E7 (274), 4B4C4 (275), 5G7D8 (276), NT2/4D5.24 (278), polyclonal (279), 2D9D5 (289), polyclonal (290), polyclonal (291), polyclonal (292)
N-term	polyclonal (259), TA9 (261), TD84 (262), TE135 (263), polyclonal (264), NT3/2D1.1 (265), 1D9D5 (267), polyclonal (270), polyclonal (271), polyclonal (279), polyclonal (290), polyclonal (291), polyclonal (292), G1 (293), G2 (294), J1 (295), TC15 (296), polyclonal (297), polyclonal (298)
Tat basic region	polyclonal (259), TB12 (268), polyclonal (270), polyclonal (271), polyclonal (272), polyclonal (279), polyclonal (290), polyclonal (291), polyclonal (292), B1E3 (299), J3B2 (300)
Env (gp160)	
C-HR	polyclonal (953)
C-domain	polyclonal (650), 5B2 (720), 9G11 (721), TH-Ab1 (722), polyclonal (723), polyclonal (724), polyclonal (725), polyclonal (726)
C-term	105-306 (620), 750-D (622), 158F3 (625), 161D7 (626), 722-D (628), polyclonal (629), 1131-A (630), 858-D (631), 989-D (632), 2F5 (717), 14D9 (727), 4E10 (728), Z13 (729), 1575 (750), polyclonal (754), polyclonal (755), 1577 (757), polyclonal (758), 101-342 (954), 101-451 (955), 120-1 (956), T26 (957), D33 (958), polyclonal (959)

Binding type	MAb ID (No.)
C1	M85 (313), 7E2/4 (314), 4D4#85 (315), M92 (316), M86 (317), polyclonal (318), 133/237 (319), 133/290 (320), 133/11 (321), D/3G5 (322), D/6A11 (323), D/5E12 (324), L5.1 (325), 4A7C6 (326), 1D10 (327), B242 (328), 133/192 (329), 489.1(961) (330), 5B3 (331), B10 (332), B2 (333), C6 (334), MF49.1 (335), T1.1 (336), T7.1 (337), T9 (338), GV4D3 (339), B27 (340), B9 (341), B35 (342), D/4B5 (343), D/5A11 (344), D/6B2 (345), B18 (346), B20 (347), MF39.1 (348), 187.2.1 (349), 37.1.1(ARP 327) (350), 6D8 (351), M96 (352), MF119.1 (353), MF4.1 (354), MF53.1 (355), MF58.1 (356), MF77.1 (357), T2.1 (358), 11/65 (359), W1 (360), T11 (361), GV1A8 (362), 11 (363), 12G10 (364), 135/9 (365), 7C10 (366), C4 (367), MF46.1 (368), 212A (960), 522-149 (961), CA1 (962), CA13 (963), L19 (964), M90 (965), MAG 104 (966), MAG 45 (967), MAG 95 (968), MAG 97 (969), P35 (970), T9 (971), p7 (972)
C1-C2	L100 (973)
C1-C4	2/11c (974), A32 (975)
C1-C5	C11 (976), L81 (977)
C2	1006-30-D (409), 847-D (410), 213.1 (414), B12 (415), B13 (416), C13 (417), M89 (418), B21 (419), B23 (420), B24 (421), B25 (422), B3 (423), B26 (424), B29 (425), B36 (426), 110.E (427), 110.C (428)
C3	2H1B (382), 110.D (568), B32 (569), ICR38.1a (580), 2F19C (760), B2C (978), polyclonal (979)
C4	5C2E5 (575), G3-211 (576), G3-537 (577), ICR38.1a (580), G3-299 (581), G3-42 (582), G3-508 (583), G3-519 (584), G3-536 (585), ICR38.8f (586), MO86/C3 (587), 13H8 (588), G45-60 (589), polyclonal (590), 1662 (591), 1663 (592), 1664 (593), 1697 (594), 1794 (595), 1804 (596), 1807 (597), 1808 (598), 1024 (980), 4KG5 (981)
C5	9201 (603), 1C1 (604), 3F5 (605), 5F4/1 (606), 660-178 (607), 9301 (608), B221 (609), H11 (611), W2 (612), M38 (613), 110.1 (616), 42F (617), 43F (618), RV110026 (619), GV1G2 (621), 450-D (623), 670-D (624), 1331A (633), 23A (982), D7324 (983)
CD4BS	JL413 (574), polyclonal (578), 1795 (579), D33 (958), polyclonal (959), 10/46c (984), 1008-D (985), 1027-30-D (986), 1125H (987), 1125H (988), 120-1B1 (989), 1202-D (990), 1331E (991), 1570 (992), 1595 (993), 1599 (994), 15e (995), 21h (996), 28A11/B1 (997), 2G6 (998), 35F3/E2 (999), 38G3/A9 (1000), 428 (1001), 448-D (1002), 46D2/D5 (1003), 48-16 (1004), 50-61A (1005), 5145A (1006), 558-D (1007), 559/64-D (1008), 55D5/F9 (1009), 588-D (1010), 654-D (1011), 67G6/C4 (1012), 729-D (1013), 830D (1014), 9CL (1015), BM12 (1016), D20 (1017), D21 (1018), D24 (1019), D25 (1020), D28 (1021), D35 (1022), D39 (1023), D42 (1024), D52 (1025), D53 (1026), D60 (1027), DA48 (1028), DO8i (1029), F105 (1030), F91 (1031), FG39 (1032), Fbb14 (1033), GP13 (1034), GP44 (1035), GP68 (1036), HF1.7 (1037), HT5 (1038), HT6 (1039), HT7 (1040), ICR 39.13g (1041), ICR 39.3b (1042), Ia3 (1043), Ia7 (1044), IgG1b12 (1045), IgGCD4 (1046), L28 (1047), L33 (1048), L41 (1049), L42 (1050), L52 (1051), L72 (1052), M12 (1053), M13 (1054), M6 (1055), MAG 116 (1056), MAG 12B (1057), MAG 29B (1058), MAG 3B (1059), MAG 55 (1060), MAG 72 (1061), MAG 86 (1062), MAG 96 (1063), MTW61D (1064), S1-1 (1065), T13 (1066), T49 (1067), T56 (1068), TH9 (1069), anti-CD4BS summary (1070), b11 (1071), b13 (1072), b14 (1073), b3 (1074), b6 (1075), polyclonal (1076), (1077)
CD4i	E51 (573), A32 (975), (1077), 17b (1078), 21c (1079), 23e (1080), 48d (1081), 49e (1082), Fbb21 (1083), Fbb21 (1084), X5 (1085), 8F101 (1086)
Env oligomer	T22 (1087)
Leucine zipper motif	(642), (643)
N-HR	polyclonal (953)

Binding type	MAb ID (No.)
N-term	polyclonal (651), D33 (958), 2A2 (1088), AC4 (1089), AD3 (1090), AD3 (1091), ID6 (1092), ID6 (1093)
V1	35D10/D2 (372), 40H2/C7 (373), 43A3/E4 (374), 43C7/B9 (375), 45D1/B7 (376), 46E3/E6 (377), 58E1/B3 (378), 64B9/A6 (379), 69D2/A1 (380), 82D3/C3 (381), polyclonal (599)
V1-V2	4KG5 (981), 11/68b (1094), 62c (1095), CRA-6 (1096), L15 (1097), T52 (1098), T54 (1099)
V1-V2 and V3-V5	polyclonal (1100)
V2	6D5 (369), B33 (370), 697-D (383), C108G (385), 11/4c (390), 8.22.2 (391), 12b (392), G3-136 (393), G3-4 (394), polyclonal (599), (1077), 1088 (1101), 110-B (1102), 1357 (1103), 1361 (1104), 1393A (1105), 2158 (1106), 66a (1107), 66c (1108), 684-238 (1109), 830A (1110), CRA-3 (1111), CRA-4 (1112), L17 (1113), SC258 (1114)
V2-CD4BS	L25 (1115), L39 (1116), L40 (1117), L78 (1118)
V3	IIIB-V3-26 (429), IIIB-V3-21 (430), 168B8 (431), polyclonal (432), polyclonal (433), MO97/V3 (434), polyclonal (435), 55/1l (436), 8/38c (437), 8/64b (438), polyclonal (439), polyclonal (440), polyclonal (441), polyclonal (442), 9284 (443), polyclonal (444), polyclonal (445), polyclonal (446), polyclonal (447), MAG 109 (448), MAG 49 (449), MAG 53 (450), MAG 56 (451), 1324-E (452), polyclonal (453), MO99/V3 (454), C311E (455), 924 (457), polyclonal (458), polyclonal (459), polyclonal (460), 10F10 (461), 2C4 (462), 412-D (463), polyclonal (464), CGP 47 439 (465), polyclonal (466), 178.1 (467), 257-D (468), 311-11-D (469), 41148D (470), 391/95-D (471), Aw (472), Bw (473), DO142-10 (474), Dv (475), Fv (476), Gv (477), Hv (478), polyclonal (479), 50.1 (480), (481), BAT123 (482), 838-D (483), 1006-15D (484), 782-D (485), 908-D (486), 1027-15D (487), F19.26-4 (488), F19.48-3 (489), F19.57-11 (490), 13105100 (491), M77 (492), polyclonal (493), SP.BAL114 (494), SP.SF2:104 (495), polyclonal (496), 19b (497), loop 2 (498), 4G10 (499), 5F7 (500), G3-523 (501), MN215 (502), Nea 9301 (503), 4117C (504), 419-D (505), 453-D (506), 504-D (507), 83.1 (508), 5023B (509), F58/D1 (510), P1/D12 (511), P4/D10 (512), IIIB-13 V3 (513), IIIB-34 V3 (514), A47/B1 (515), D59/A2 (516), G44/H7 (517), MO96/V3 (518), μ5.5 (519), 268-D (520), 386-D (521), 5042A (522), 5042B (523), 418-D (524), 5021 (525), 5025B (526), 5042 (527), 110.3 (528), 110.4 (529), 110.5 (530), 58.2 (531), 537-D (533), 5020 (534), RC25 (535), 5023A (536), 110.6 (537), polyclonal (538), 10/36e (539), 10/54 (540), 11/85b (541), polyclonal (542), 0.5β (543), Cβ1, 0.5β (544), NM-01 (545), 1026 (546), 1034 (547), 59.1 (548), polyclonal (549), 10E3 (550), polyclonal (551), N11-20 (552), 5025A (553), N70-1.9b (554), 902 (555), 694/98-D (556), 9205 (560), 110.I (561), anti-HIV-2 polyclonal (562), IIIB-V3-01 (563), polyclonal (599), 447-52D (733), 1334-D (761), 4KG5 (981), (1077), (1119), 10D8 (1120), 10F6 (1121), 110.J (1122), 11G5 (1123), 2182 (1124), 2191 (1125), 2219 (1126), 2412 (1127), 2442 (1128), 2456 (1129), 2483 (1130), 2497 (1131), 2557 (1132), 2558 (1133), 2580 (1134), 391/95-D (1135), 39F (1136), 4148d (1137), 55/68b (1138), 5G11 (1139), 6.1 (1140), 6.7 (1141), 8.27.3 (1142), 8E11/A8 (1143), 9305 (1144), A1g8 (1145), AG1121 (1146), Ag1211 (1147), B4a1 (1148), B4e8 (1149), D27 (1150), D47 (1151), D56 (1152), F5.5 (1153), G3-1472 (1154), K24 (1155), TH1 (1156), anti-gp120/V3 (1157), polyclonal (1158), polyclonal (1159), polyclonal (1160), polyclonal (1161), polyclonal (1162), polyclonal (1163), polyclonal (1164), polyclonal (1165), polyclonal (1166), polyclonal (1172)
V3 discontinuous	11/75a/21/41 (1167), 41.1 (1168), 55/45a/1l (1169)
V3 mimotope	1108 (1170)
V3-C4	MO101/V3,C4 (557), polyclonal (959), polyclonal (1171)
V3-C5	MO101/V3,C4 (558), MO101/V3,C4 (559)

Binding type	MAb ID (No.)
V4	D/6D1 (564), 4D7/4 (565), 36.1(ARP 329) (566), C12 (567), polyclonal (570), B15 (571), B34 (572), polyclonal (599), polyclonal (1172)
V5	polyclonal (599), polyclonal (600)
V5-C5	CRA1(ARP 323) (601), M91 (602), 8C6/1 (610)
adjacent to cluster II	2F5 (717), 14D9 (727)
alpha-helical hairpin intermediate	98-6 (713), polyclonal (1173)
carbohydrates at glycosylation residues in C2, C3, C4, and V4	2G12 (1174)
cluster I	50-69 (655), 246-D (673), 181-D (676), 240-D (677), F240 (678), D49 (679), D61 (680), T32 (681), T34 (682), 3D6 (709), 1367 (1175), 7B2 (1176)
cluster II	98-6 (713), 167-7 (714), ND-15G1 (715), 167-D (716), D50 (763), 126-6 (1177), 1342 (1178), 1379 (1179), 2.2B (1180), Fab D11 (1181), Fab D5 (1182), Fab G1 (1183), Fab M10 (1184), Fab M12 (1185), Fab M15 (1186), Fab S10 (1187), Fab S6 (1188), Fab S8 (1189), Fab S9 (1190), Fab T3 (1191), Md-1 (1192), 1281 (1199)
cluster III	Fab A9 (1193), Fab G15 (1194), Fab G5 (1195), Fab L1 (1196), Fab L11 (1197), Fab L2 (1198)
cytoplasmic domain	Chessie 8 (1200)
gp120-CD4 complex	8F101 (1086), 8F102 (1201), CG-10 (1202), CG-25 (1203), CG-4 (1204), CG-76 (1205), CG-9 (1206)
immunodominant region	3D6 (709), 105-518 (1207)
p24+gp41	31A1 (1208), 39A64 (1209), 39B86 (1210), 9303 (1211)
six-helix bundle	167-D (716), polyclonal (953), 1281 (1199), NC-1 (1212)
Nef	
C-term	AE6 (1253), AG11 (1254), EH1 (1255), AE6 (1263)

IV-B-2 Alphabetical listing of MAbs

Cross reference of MAb names and their order of appearance in the tables. Alphanumeric sorting is symbols, digits and letters.

MAb ID	No.
	280
	481
	642
	643
	652
	764
	765
	766
	767
	768
	1077
	1119
	1264
α(566-586)	638
μ5.5	519
0.5β	543
1-B-7	68
1-E-4	57
1-E-9	58
1.152 B3	182
1.153 G10	190
1.158 E2	183
1.160 B3	194
1.17.3	89
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10/76b	386
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1027-30-D	986
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105-306	620
105-518	1207
105-732	708
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10E7	174
10E9	772
10F10	461
10F6	1121
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1393A	1105
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14D9	727
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1570	992
1575	750
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1577	757
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1583	740
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1595	993
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1664	593
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17	216
178.1	467
1794	595
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17b	1078
1804	596
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1A7	90
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1B8.env	697
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1G10	309
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2158	1106
2182	1124
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21c	1079
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2219	1126
23A	982
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25C2 636
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39B86 1210
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42F 617
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450-D 623
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4G2 649
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6E9	199	908-D	486	B15	571	CA1	962
6G5	211	91-5	48	B18	346	CA13	963
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71-31	139	9205	560	B20	347	CD-4/1	44
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74	397	9303	1211	B24	421	CG-25	1203
75	706	9305	1144	B242	328	CG-4	1204
750-D	622	97B1/E8	801	B25	422	CG-76	1205
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7B2	1176	98-4.9	142	B27	340	CGP 47 439	465
7B6	212	98-43	657	B29	425	CH9B2	147
7C10	366	98-6	713	B2C	978	Chessie 8	1200
7C3	228	989-D	632	B3	423	Chim 1	614
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7C4	244	9CL	1015	B30	730	CRA-3	1111
7C6	213	9G11	721	B31	735	CRA-4	1112
7E2/4	314	9G2	306	B32	569	CRA-6	1096
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8-6	222	A32	975	B35	342	D/5A11	344
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8-D-5	72	A6	1217	B4	806	D/6A11	323
8-G-9	65	A7	1220	B4a1	1148	D/6B2	345
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8.22.2	391	Ab2	302	B4f8	16	D1	813
8.27.3	1142	Ab3	311	B5	807	D12	814
8/38c	437	Ab4	307	B6	808	D16	815
8/64b	438	AC2	143	b6	1075	D20	1017
82D3/C3	381	AC4	1089	B8	756	D21	1018
83.1	508	AD2	126	B9	341	D24	1019
830A	1110	AD3	1090	BAT085	395	D25	1020
830D	1014	AD3	1091	BAT123	482	D27	1150
838-D	483	ADP421 polyclonal	803	BAT267	809	D28	1021
847-D	410	AE6	1253	BAT401	810	D33	958
858-D	631	AE6	1263	BAT509	811	D35	1022
85G11/D8	799	AG10H9	804	BC1071	144	D39	1023
86	666	AG11	1254	BE10	145	D4	816
87E4/A8	800	AG1121	1146	BE3	108	D42	1024
88-158/02	751	Ag1211	1147	BM12	1016	D43	817
88-158/022	752	AH48	805	Bw	473	D47	1151
88-158/079	753	AM5C6	1218	Cβ1, 0.5β	544	D49	679
8B11	177	AM5C6	1219	C108G	385	D50	763
8C10	178	anti-HIV-1 RT	248	C11	976	D52	1025
8C6/1	610	anti-HIV-2 polyclonal	562	C12	567	D53	1026
8E11/A8	1143	anti-CD4BS summary	1070	C13	417	D56	1152
8E5	230	anti-gp120/V3	1157	C2003	196	D59/A2	516
8E7	305	anti-K159	220	C31	812	D60	1027
8F101	1086	anti-p24	155	C311E	455	D61	680
8F102	1201	Aw	472	C4	367	D7324	983
8G4	215	B10	332	C5122	103	DA48	1028
8G5	179	b11	1071	C5123	67	DF3	128
8H10	14	B12	415	C5126	27	DG8	123

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Dv	475	Fab S6	1188	HyHIV-3	7	LH-104-E	85
DZ	759	Fab S8	1189	HyHIV-4	8	LH-104-G	119
E-4	200	Fab S9	1190	HyHIV-5	9	LH-104-I	118
E5	1245	Fab T2	665	HyHIV-6	10	LH-104-K	87
E51	573	Fab T3	1191	i5B11	120	loop 2	498
E7	1252	Fbb14	1033	Ia3	1043	M-1	684
E9	1243	Fbb21	1083	Ia7	1044	M-11	685
EB1A9	81	Fbb21	1084	ICR 39.13g	1041	M-13	686
EB5	124	FC12	130	ICR 39.3b	1042	M-2	687
EC3	129	FF1	73	ICR38.1a	580	M-22	688
EC6	121	FG39	1032	ICR38.8f	586	M-24	689
ED6	748	FH2	114	ID6	1092	M-25	690
ED8	148	Fv	476	ID6	1093	M-28	691
EF7	84	G1	293	ID8F6	39	M-29	692
EH1	1255	G11G1	150	IE8G2	153	M-36	693
EH12E1	149	G11H3	151	IgA6/30lambda	831	M-4	694
F-6	253	G12	824	IgA6/5k	832	M-6	695
F1	1241	G2	294	IgA6/L4	833	M12	122
F105	1030	G2	825	IgG1b12	1045	M12	1053
F11.2.32	175	G3-136	393	IgGCD4	1046	M13	1054
F14.11	1232	G3-1472	1154	IIIB-13 V3	513	m18	850
F172-D8	710	G3-211	576	IIIB-34 V3	514	M25	835
F19.26-4	488	G3-299	581	IIIB-V3-01	563	M38	613
F19.48-3	489	G3-4	394	IIIB-V3-21	430	M6	1055
F19.57-11	490	G3-42	582	IIIB-V3-26	429	M77	492
F2	1235	G3-508	583	IVI-4G6	830	M85	313
F223	818	G3-519	584	J1	295	M86	317
F240	678	G3-523	501	J1	407	M89	418
F285	819	G3-536	585	J3	408	M90	965
F3	1239	G3-537	577	J3B2	300	M91	602
F4	1234	G44/H7	517	J4	256	M92	316
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F58/D1	510	GP44	1035	K14	834	MAG 109	448
F7	820	GP68	1036	K24	1155	MAG 116	1056
F8	1240	Gv	477	L-anti-Tat	281	MAG 12B	1057
F91	1031	GV1A8	362	L100	973	MAG 29B	1058
Fab A1	660	GV1G2	621	L14	109	MAG 3B	1059
Fab A12	821	GV4D3	339	L14.17	1	MAG 45	967
Fab A2	822	GV4H3	406	L15	1097	MAG 49	449
Fab A4	661	H11	611	L17	1113	MAG 53	450
Fab A9	1193	H2	826	L19	964	MAG 55	1060
Fab D11	1181	H8	827	L25	1115	MAG 56	451
Fab D5	1182	HBW4	828	L28	1047	MAG 6B	836
Fab G1	1183	HF1.7	1037	L33	1048	MAG 72	1061
Fab G15	1194	HH3	125	L39	1116	MAG 86	1062
Fab G5	1195	HIVIG	829	L40	1117	MAG 95	968
Fab L1	1196	HT5	1038	L41	1049	MAG 96	1063
Fab L11	1197	HT6	1039	L42	1050	MAG 97	969
Fab L2	1198	HT7	1040	L5.1	325	Md-1	1192
Fab L9	823	human sera	156	L52	1051	MF119.1	353
Fab M10	1184	Hv	478	L72	1052	MF169.1	411
Fab M12	1185	HyHIV-1	5	L78	1118	MF170.1	412
Fab M12B	662	HyHIV-15	24	L81	977	MF39.1	348
Fab M15	1186	HyHIV-19	152	LA9 (121-134)	749	MF4.1	354
Fab M26B	663	HyHIV-2	6	LH-104-A	88	MF46.1	368

MF49.1	335	polyclonal	164	polyclonal	496	polyclonal	878
MF53.1	355	polyclonal	165	polyclonal	532	polyclonal	879
MF58.1	356	polyclonal	166	polyclonal	538	polyclonal	880
MF77.1	357	polyclonal	167	polyclonal	542	polyclonal	881
MF87.1	413	polyclonal	168	polyclonal	549	polyclonal	882
MN215	502	polyclonal	169	polyclonal	551	polyclonal	883
MO101/V3,C4	557	polyclonal	170	polyclonal	570	polyclonal	884
MO101/V3,C4	558	polyclonal	171	polyclonal	578	polyclonal	885
MO101/V3,C4	559	polyclonal	181	polyclonal	590	polyclonal	886
MO28	837	polyclonal	189	polyclonal	599	polyclonal	887
MO30	838	polyclonal	195	polyclonal	600	polyclonal	888
MO43	839	polyclonal	249	polyclonal	615	polyclonal	889
MO86/C3	587	polyclonal	250	polyclonal	627	polyclonal	890
MO9.42.2	97	polyclonal	251	polyclonal	629	polyclonal	891
MO9.50.2	98	polyclonal	257	polyclonal	641	polyclonal	892
MO96/V3	518	polyclonal	258	polyclonal	650	polyclonal	893
MO97/V3	434	polyclonal	259	polyclonal	651	polyclonal	894
MO99/V3	454	polyclonal	260	polyclonal	653	polyclonal	895
MTW61D	1064	polyclonal	264	polyclonal	667	polyclonal	896
multiple Fabs	851	polyclonal	269	polyclonal	669	polyclonal	897
multiple MAbs	852	polyclonal	270	polyclonal	670	polyclonal	898
multiple MAbs	853	polyclonal	271	polyclonal	671	polyclonal	899
multiple MAbs	854	polyclonal	272	polyclonal	674	polyclonal	900
N11-20	552	polyclonal	277	polyclonal	698	polyclonal	901
N2-4	840	polyclonal	279	polyclonal	699	polyclonal	902
N70-1.9b	554	polyclonal	282	polyclonal	707	polyclonal	903
N70-2.3a	841	polyclonal	283	polyclonal	718	polyclonal	904
NC-1	1212	polyclonal	284	polyclonal	719	polyclonal	905
ND-15G1	715	polyclonal	285	polyclonal	723	polyclonal	906
Nea 9301	503	polyclonal	286	polyclonal	724	polyclonal	907
NF1A1	1250	polyclonal	287	polyclonal	725	polyclonal	908
NF2B2	1259	polyclonal	288	polyclonal	726	polyclonal	909
NF3A3	1260	polyclonal	290	polyclonal	731	polyclonal	910
NF8B4	1261	polyclonal	291	polyclonal	754	polyclonal	911
NM-01	545	polyclonal	292	polyclonal	755	polyclonal	912
NT2/4D5.24	278	polyclonal	297	polyclonal	758	polyclonal	913
NT3/2D1.1	265	polyclonal	298	polyclonal	855	polyclonal	914
P1/D12	511	polyclonal	318	polyclonal	856	polyclonal	915
P35	970	polyclonal	371	polyclonal	857	polyclonal	916
P4/D10	512	polyclonal	400	polyclonal	858	polyclonal	917
P43110	842	polyclonal	432	polyclonal	859	polyclonal	918
P5-3	843	polyclonal	433	polyclonal	860	polyclonal	919
p7	972	polyclonal	435	polyclonal	861	polyclonal	920
PC5009	639	polyclonal	439	polyclonal	862	polyclonal	921
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polyclonal	158	polyclonal	459	polyclonal	872	polyclonal	931
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polyclonal	161	polyclonal	466	polyclonal	875	polyclonal	934
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polyclonal	1251
polyclonal	1262
polyclonal	1265
polyclonal	1266
polyclonal	1267
polyclonal	1268
polyclonal	1269
polyclonal	1270
polyclonal	1271
polyclonal	1272
polyclonal	1273
polyclonal α577-596	640
polyclonal α598-609	696
polyclonal HIVIG	172
RC25	535
RL4.72.1	77
RSD-33	389
RT-4	245
RT6H	193
RT7O	246
RT7U	247
RTMAb8	191
RV110026	619
S1-1	1065
sc-FV p17	34
SC258	1114
SP.BAL114	494
SP.SF2:104	495
T1.1	336
T11	361
T13	1066
T15G1	844
T2.1	358
T20	845
T22	1087
T26	957
T27	846
T3	847
T30	848
T32	681
T34	682
T4	849
T49	1067
T52	1098
T54	1099
T56	1068
T7.1	337
T9	338
T9	971
TA9	261
TB12	268
TC15	296
TD84	262
TE135	263
TG001	255
TG002	254
TH-Ab1	722
TH1	1156
TH9	1069
V10	99
V10-9	668
V107	100
V7-8	154
W1	360
W2	612
X5	1085
Z13	729

IV-B-3 MAbs by order of appearance in tables

No.	MAb ID
p17	
1	L14.17
2	polyclonal
3	32/5.8.42
4	32/5.8.42
5	HyHIV-1
6	HyHIV-2
7	HyHIV-3
8	HyHIV-4
9	HyHIV-5
10	HyHIV-6
11	32/1.24.89
12	3B10
13	3E11
14	8H10
15	HyHIV-21
16	B4f8
17	HyHIV-22
18	12H-D3b3
19	12G-A8g2
20	12G-D7h11
21	12G-H1c7
22	12I-D12g2
23	polyclonal
24	HyHIV-15
25	11H9
26	3-H-7
27	C5126
28	1D9
29	4C9
30	4H2B1
31	9G5
32	15-21
33	31-11
34	sc-FV p17
p17-p24	
35	3A6
p24	
36	111/182
37	112/021
38	112/047
39	ID8F6
40	F5-2
41	CB-13/5
42	polyclonal
43	3D3
44	CD-4/1
45	15F8C7
46	111/052
47	polyclonal
48	91-5
49	1109/01
50	14D4E11
51	1G5C8
52	47-2
53	714/01
54	polyclonal
55	111/073
56	113/038
57	1-E-4
58	1-E-9
59	10-E-7
60	10-G-9
61	11-C-5
62	2-E-4
63	2-H-4
64	8-D-2
65	8-G-9
66	8-H-7
67	C5123
68	1-B-7
69	3-B-7
70	6-D-12
71	6-E-7
72	8-D-5
73	FF1
74	113/072
75	25.3
76	13-102-100
77	RL4.72.1
78	406/01
79	polyclonal
80	38:9.6K
81	EB1A9
82	polyclonal
83	30:3E5
84	EF7
85	LH-104-E
86	1B2C12
87	LH-104-K
88	LH-104-A
89	1.17.3
90	1A7
91	1F6
92	23A5G4
93	23A5G5
94	3D10G6
95	polyclonal
96	F5-4
97	MO9.42.2
98	MO9.50.2
99	V10
100	V107
101	LH-104-C
102	12-B-4
103	C5122
104	9A4C4
105	11C10B10
106	11D11F2
107	CD12B4
108	BE3
109	L14
110	108/03
111	110/015
112	32:32K
113	C5200
114	FH2
115	13B5
116	106/01
117	LH-104-B
118	LH-104-I
p24-p2p7p1p6	
119	LH-104-G
p2p7p1p6	
120	i5B11
121	EC6
122	M12
123	DG8
124	EB5
125	HH3
126	AD2
127	CA5
128	DF3
129	EC3
130	FC12
131	GE4
132	JB7
133	JF11
Gag	
134	16/4/2
135	183-H12-5C
136	241-D
137	2A6
138	5E2.A3k
139	71-31
140	91-6
141	98-4.3
142	98-4.9
143	AC2
144	BC1071
145	BE10
146	CD9
147	CH9B2
148	ED8
149	EH12E1
150	G11G1
151	G11H3
152	HyHIV-19
153	IE8G2
154	V7-8
155	anti-p24
156	human sera
157	polyclonal
158	polyclonal
159	polyclonal
160	polyclonal
161	polyclonal
162	polyclonal
163	polyclonal
164	polyclonal
165	polyclonal
166	polyclonal
167	polyclonal
168	polyclonal
169	polyclonal
170	polyclonal
171	polyclonal
172	polyclonal HIVIG
Protease	
173	1696
174	10E7
175	F11.2.32
176	13E1
177	8B11
178	8C10
179	8G5
RT	
180	1E8
181	polyclonal
182	1.152 B3
183	1.158 E2
184	31D6
185	31G8
186	32E7
187	33D5
188	5B2
189	polyclonal
190	1.153 G10
191	RTMAb8
192	1D4A3
193	RT6H
194	1.160 B3
195	polyclonal
196	C2003
197	5B11
198	6B10
199	6E9
200	E-4
201	6B9
202	5F
203	5G
204	7C4
Integrase	
205	1C4
206	2C11
207	2E3
208	3E11
209	3F9
210	5F8
211	6G5
212	7B6
213	7C6
214	6C5
215	8G4
216	17
217	4D6
218	7-16

219 4F6
220 anti-K159
221 5D9
222 8-6
223 19
224 2-19
225 8-22
226 4-20
227 6-19
228 7C3
229 7F11
230 8E5
231 MAb 35
Pol
232 12
233 13
234 14
235 16
236 1C12B1
237 21
238 32
239 35
240 3D12
241 3F10
242 4
243 6B9
244 7C4
245 RT-4
246 RT7O
247 RT7U
248 anti-HIV-1 RT
249 polyclonal
250 polyclonal
251 polyclonal
252 33
253 F-6
Vif
254 TG002
255 TG001
256 J4
257 polyclonal
Vpr
258 polyclonal
Tat
259 polyclonal
260 polyclonal
261 TA9
262 TD84
263 TE135
264 polyclonal
265 NT3/2D1.1
266 1.2
267 1D9D5
268 TB12
269 polyclonal
270 polyclonal
271 polyclonal
272 polyclonal
273 1D2F11
274 2D9E7
275 4B4C4
276 5G7D8
277 polyclonal
278 NT2/4D5.24
279 polyclonal
280
281 L-anti-Tat
282 polyclonal
283 polyclonal
284 polyclonal
285 polyclonal
286 polyclonal
287 polyclonal
288 polyclonal
289 2D9D5
290 polyclonal
291 polyclonal
292 polyclonal
293 G1
294 G2
295 J1
296 TC15
297 polyclonal
298 polyclonal
299 B1E3
300 J3B2
Rev
301 4G9
302 Ab2
303 10.1
304 3H6
305 8E7
306 9G2
307 Ab4
308 3G4
309 1G10
310 1G7
311 Ab3
312 2G2
gp160
313 M85
314 7E2/4
315 4D4#85
316 M92
317 M86
318 polyclonal
319 133/237
320 133/290
321 133/11
322 D/3G5
323 D/6A11
324 D/5E12
325 L5.1
326 4A7C6
327 1D10
328 B242
329 133/192
330 489.1(961)
331 5B3
332 B10
333 B2
334 C6
335 MF49.1
336 T1.1
337 T7.1
338 T9
339 GV4D3
340 B27
341 B9
342 B35
343 D/4B5
344 D/5A11
345 D/6B2
346 B18
347 B20
348 MF39.1
349 187.2.1
350 37.1.1(ARP 327)
351 6D8
352 M96
353 MF119.1
354 MF4.1
355 MF53.1
356 MF58.1
357 MF77.1
358 T2.1
359 11/65
360 W1
361 T11
362 GV1A8
363 11
364 12G10
365 135/9
366 7C10
367 C4
368 MF46.1
369 6D5
370 B33
371 polyclonal
372 35D10/D2
373 40H2/C7
374 43A3/E4
375 43C7/B9
376 45D1/B7
377 46E3/E6
378 58E1/B3
379 64B9/A6
380 69D2/A1
381 82D3/C3
382 2H1B
383 697-D
384 6C4/S
385 C108G
386 10/76b
387 11/41e
388 11/4b
389 RSD-33
390 11/4c
391 8.22.2
392 12b
393 G3-136
394 G3-4
395 BAT085
396 60b
397 74
398 38/12b
399 38/60b
400 polyclonal
401 322-151
402 3D3.B8
403 4C11.D8
404 493-156
405 110.1
406 GV4H3
407 J1
408 J3
409 1006-30-D
410 847-D
411 MF169.1
412 MF170.1
413 MF87.1
414 213.1
415 B12
416 B13
417 C13
418 M89
419 B21
420 B23
421 B24
422 B25
423 B3
424 B26
425 B29
426 B36
427 110.E
428 110.C
429 IIIB-V3-26
430 IIIB-V3-21
431 168B8
432 polyclonal
433 polyclonal
434 MO97/V3
435 polyclonal
436 55/1l
437 8/38c
438 8/64b
439 polyclonal
440 polyclonal
441 polyclonal
442 polyclonal
443 9284
444 polyclonal
445 polyclonal
446 polyclonal
447 polyclonal
448 MAG 109

449 MAG 49
450 MAG 53
451 MAG 56
452 1324-E
453 polyclonal
454 MO99/V3
455 C311E
456 907
457 924
458 polyclonal
459 polyclonal
460 polyclonal
461 10F10
462 2C4
463 412-D
464 polyclonal
465 CGP 47 439
466 polyclonal
467 178.1
468 257-D
469 311-11-D
470 41148D
471 391/95-D
472 Aw
473 Bw
474 DO142-10
475 Dv
476 Fv
477 Gv
478 Hv
479 polyclonal
480 50.1
481
482 BAT123
483 838-D
484 1006-15D
485 782-D
486 908-D
487 1027-15D
488 F19.26-4
489 F19.48-3
490 F19.57-11
491 13105100
492 M77
493 polyclonal
494 SP.BAL114
495 SP.SF2:104
496 polyclonal
497 19b
498 loop 2
499 4G10
500 5F7
501 G3-523
502 MN215
503 Nea 9301
504 4117C
505 419-D
506 453-D
507 504-D
508 83.1
509 5023B
510 F58/D1
511 P1/D12
512 P4/D10
513 IIIB-13 V3
514 IIIB-34 V3
515 A47/B1
516 D59/A2
517 G44/H7
518 MO96/V3
519 μ5.5
520 268-D
521 386-D
522 5042A
523 5042B
524 418-D
525 5021
526 5025B
527 5042
528 110.3
529 110.4
530 110.5
531 58.2
532 polyclonal
533 537-D
534 5020
535 RC25
536 5023A
537 110.6
538 polyclonal
539 10/36e
540 10/54
541 11/85b
542 polyclonal
543 0.5β
544 Cβ1, 0.5β
545 NM-01
546 1026
547 1034
548 59.1
549 polyclonal
550 10E3
551 polyclonal
552 N11-20
553 5025A
554 N70-1.9b
555 902
556 694/98-D
557 MO101/V3,C4
558 MO101/V3,C4
559 MO101/V3,C4
560 9205
561 110.I
562 anti-HIV-2 polyclonal
563 IIIB-V3-01
564 D/6D1
565 4D7/4
566 36.1(ARP 329)
567 C12
568 110.D
569 B32
570 polyclonal
571 B15
572 B34
573 E51
574 JL413
575 5C2E5
576 G3-211
577 G3-537
578 polyclonal
579 1795
580 ICR38.1a
581 G3-299
582 G3-42
583 G3-508
584 G3-519
585 G3-536
586 ICR38.8f
587 MO86/C3
588 13H8
589 G45-60
590 polyclonal
591 1662
592 1663
593 1664
594 1697
595 1794
596 1804
597 1807
598 1808
599 polyclonal
600 polyclonal
601 CRA1(ARP 323)
602 M91
603 9201
604 1C1
605 3F5
606 5F4/1
607 660-178
608 9301
609 B221
610 8C6/1
611 H11
612 W2
613 M38
614 Chim 1
615 polyclonal
616 110.1
617 42F
618 43F
619 RV110026
620 105-306
621 GV1G2
622 750-D
623 450-D
624 670-D
625 158F3
626 161D7
627 polyclonal
628 722-D
629 polyclonal
630 1131-A
631 858-D
632 989-D
633 1331A
634 1A1
635 24G3
636 25C2
637 5F3
638 α(566-586)
639 PC5009
640 polyclonal α577-596
641 polyclonal
642
643
644 1F11
645 1H5
646 3D9
647 4B3
648 4D4
649 4G2
650 polyclonal
651 polyclonal
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653 polyclonal
654 2A2/26
655 50-69
656 9-11
657 98-43
658 41-1
659 41.4
660 Fab A1
661 Fab A4
662 Fab M12B
663 Fab M26B
664 Fab M8B
665 Fab T2
666 86
667 polyclonal
668 V10-9
669 polyclonal
670 polyclonal
671 polyclonal
672 2F11
673 246-D
674 polyclonal
675 9G5A
676 181-D
677 240-D
678 F240
679 D49
680 D61
681 T32
682 T34
683 115.8
684 M-1

685 M-11
686 M-13
687 M-2
688 M-22
689 M-24
690 M-25
691 M-28
692 M-29
693 M-36
694 M-4
695 M-6
696 polyclonal α598-609
697 1B8.env
698 polyclonal
699 polyclonal
700 clone 3
701 4
702 41-6
703 41-7
704 68.1
705 68.11
706 75
707 polyclonal
708 105-732
709 3D6
710 F172-D8
711 5-21-3
712 120-16
713 98-6
714 167-7
715 ND-15G1
716 167-D
717 2F5
718 polyclonal
719 polyclonal
720 5B2
721 9G11
722 TH-Ab1
723 polyclonal
724 polyclonal
725 polyclonal
726 polyclonal
727 14D9
728 4E10
729 Z13
730 B30
731 polyclonal
732 41S-2
733 447-52D
734 C8
735 B31
736 B33
737 1576
738 1578
739 1579
740 1583
741 1899
742 1907
743 1908
744 1909
745 41-1
746 41-2
747 41-3
748 ED6
749 LA9 (121-134)
750 1575
751 88-158/02
752 88-158/022
753 88-158/079
754 polyclonal
755 polyclonal
756 B8
757 1577
758 polyclonal
759 DZ
760 2F19C
761 1334-D

Env

762 7F11
763 D50
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769 102-135
770 1025
771 105-134
772 10E9
773 126-50
774 12H2
775 13.10
776 1B1
777 1D10
778 1F7
779 30D
780 31710B
781 38B5/C9
782 39H10/A11
783 3C9
784 3D5
785 3H6
786 40D3/C11
787 49B11/A1
788 52G5/B9
789 55E4/H1
790 56C4/C8
791 57B6/F1
792 57H5/D7
793 63G4/E2
794 65B12/C5
795 694/98D
796 6D8
797 6E10
798 7-1054
799 85G11/D8
800 87E4/A8
801 97B1/E8
802 A9
803 ADP421 polyclonal
804 AG10H9
805 AH48
806 B4
807 B5
808 B6
809 BAT267
810 BAT401
811 BAT509
812 C31
813 D1
814 D12
815 D16
816 D4
817 D43
818 F223
819 F285
820 F7
821 Fab A12
822 Fab A2
823 Fab L9
824 G12
825 G2
826 H2
827 H8
828 HBW4
829 HIVIG
830 IVI-4G6
831 IgA6/30lambda
832 IgA6/5k
833 IgA6/L4
834 K14
835 M25
836 MAG 6B
837 MO28
838 MO30
839 MO43
840 N2-4
841 N70-2.3a
842 P43110
843 P5-3
844 T15G1
845 T20
846 T27
847 T3
848 T30
849 T4
850 m18
851 multiple Fabs
852 multiple MAbs
853 multiple MAbs
854 multiple MAbs
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951 polyclonal
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953 polyclonal
954 101-342
955 101-451
956 120-1
957 T26
958 D33
959 polyclonal
960 212A
961 522-149
962 CA1
963 CA13
964 L19
965 M90
966 MAG 104
967 MAG 45
968 MAG 95
969 MAG 97
970 P35
971 T9
972 p7
973 L100
974 2/11c
975 A32
976 C11
977 L81
978 B2C
979 polyclonal
980 1024
981 4KG5
982 23A
983 D7324
984 10/46c
985 1008-D
986 1027-30-D
987 1125H
988 1125H
989 120-1B1
990 1202-D
991 1331E
992 1570
993 1595
994 1599
995 15e
996 21h
997 28A11/B1
998 2G6
999 35F3/E2
1000 38G3/A9
1001 428
1002 448-D
1003 46D2/D5
1004 48-16
1005 50-61A
1006 5145A
1007 558-D
1008 559/64-D
1009 55D5/F9
1010 588-D
1011 654-D
1012 67G6/C4
1013 729-D
1014 830D
1015 9CL
1016 BM12
1017 D20
1018 D21
1019 D24
1020 D25
1021 D28
1022 D35
1023 D39
1024 D42
1025 D52
1026 D53
1027 D60
1028 DA48
1029 DO8i
1030 F105
1031 F91
1032 FG39
1033 Fbb14
1034 GP13
1035 GP44
1036 GP68
1037 HF1.7
1038 HT5
1039 HT6
1040 HT7
1041 ICR 39.13g
1042 ICR 39.3b
1043 Ia3
1044 Ia7
1045 IgG1b12
1046 IgGCD4
1047 L28
1048 L33
1049 L41
1050 L42
1051 L52
1052 L72
1053 M12
1054 M13
1055 M6
1056 MAG 116
1057 MAG 12B
1058 MAG 29B
1059 MAG 3B
1060 MAG 55
1061 MAG 72
1062 MAG 86
1063 MAG 96
1064 MTW61D
1065 S1-1
1066 T13
1067 T49
1068 T56
1069 TH9
1070 anti-CD4BS summary
1071 b11
1072 b13
1073 b14
1074 b3
1075 b6
1076 polyclonal
1077
1078 17b
1079 21c
1080 23e
1081 48d
1082 49e
1083 Fbb21
1084 Fbb21
1085 X5
1086 8F101
1087 T22
1088 2A2
1089 AC4
1090 AD3
1091 AD3
1092 ID6
1093 ID6
1094 11/68b
1095 62c
1096 CRA-6
1097 L15
1098 T52
1099 T54
1100 polyclonal
1101 1088
1102 110-B
1103 1357
1104 1361
1105 1393A
1106 2158
1107 66a
1108 66c
1109 684-238
1110 830A
1111 CRA-3
1112 CRA-4
1113 L17
1114 SC258
1115 L25
1116 L39
1117 L40
1118 L78
1119
1120 10D8
1121 10F6
1122 110.J
1123 11G5
1124 2182
1125 2191
1126 2219
1127 2412
1128 2442
1129 2456
1130 2483
1131 2497
1132 2557
1133 2558
1134 2580
1135 391/95-D
1136 39F
1137 4148d
1138 55/68b
1139 5G11
1140 6.1
1141 6.7
1142 8.27.3
1143 8E11/A8
1144 9305
1145 A1g8
1146 AG1121
1147 Ag1211
1148 B4a1
1149 B4e8
1150 D27
1151 D47
1152 D56
1153 F5.5
1154 G3-1472
1155 K24

1156 TH1
1157 anti-gp120/V3
1158 polyclonal
1159 polyclonal
1160 polyclonal
1161 polyclonal
1162 polyclonal
1163 polyclonal
1164 polyclonal
1165 polyclonal
1166 polyclonal
1167 11/75a/21/41
1168 41.1
1169 55/45a/1l
1170 1108
1171 polyclonal
1172 polyclonal
1173 polyclonal
1174 2G12
1175 1367
1176 7B2
1177 126-6
1178 1342
1179 1379
1180 2.2B
1181 Fab D11
1182 Fab D5
1183 Fab G1
1184 Fab M10
1185 Fab M12
1186 Fab M15
1187 Fab S10
1188 Fab S6
1189 Fab S8
1190 Fab S9
1191 Fab T3
1192 Md-1
1193 Fab A9
1194 Fab G15
1195 Fab G5
1196 Fab L1
1197 Fab L11
1198 Fab L2
1199 1281
1200 Chessie 8
1201 8F102
1202 CG-10
1203 CG-25
1204 CG-4
1205 CG-76
1206 CG-9
1207 105-518
1208 31A1
1209 39A64
1210 39B86
1211 9303
1212 NC-1

Nef

1213 4H4
1214 polyclonal
1215 13/042
1216 13/035
1217 A6
1218 AM5C6
1219 AM5C6
1220 A7
1221 25/03
1222 26/76
1223 3F2
1224 3D12
1225 polyclonal
1226 polyclonal
1227 3G12
1228 13/058
1229 26/028
1230 2E3
1231 polyclonal
1232 F14.11
1233 31/03
1234 F4
1235 F2
1236 polyclonal
1237 polyclonal
1238 polyclonal
1239 F3
1240 F8
1241 F1
1242 2F2
1243 E9
1244 3E6
1245 E5
1246 2A3
1247 2E4
1248 2H12
1249 3A2
1250 NF1A1
1251 polyclonal
1252 E7
1253 AE6
1254 AG11
1255 EH1
1256 3B4B
1257 3H3E
1258 6.1
1259 NF2B2
1260 NF3A3
1261 NF8B4
1262 polyclonal
1263 AE6

HIV-1

1264
1265 polyclonal
1266 polyclonal
1267 polyclonal
1268 polyclonal
1269 polyclonal
1270 polyclonal
1271 polyclonal
1272 polyclonal
1273 polyclonal

IV-C

HIV Antibodies Tables

All HIV MAbs and polyclonal Abs that bind to linear epitopes 30 amino acids or less in length are arranged by protein position. The table entries are sorted in a nested way—first by protein, then by HXB2 start location, then by antibody type and finally by antibody name. Abs that bind to conformational epitopes or with unknown epitopes are listed at the end of each protein section.

IV-C-1 Gag p17 Antibodies

No. 1
MAb ID L14.17
HXB2 Location p17 (11–25)
Author Location p17 (11–25 BRU)
Epitope GELDRWEKIRLRPGG
Neutralizing no
Immunogen Vaccine
Vector/Type: viral lysate *Strain:* B clade BRU *HIV component:* HIV-1
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b; Tatsumi *et al.* 1990

No. 2
MAb ID polyclonal
HXB2 Location p17 (11–25)
Author Location p17 (11–25 LAI)
Epitope GELDRWEKIRLRPGG
Subtype B
Neutralizing N
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse
References Truong *et al.* 1997

- An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a differentantigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. Truong *et al.* [1997]

No. 3
MAb ID 32/5.8.42
HXB2 Location p17 (12–19)
Author Location p17 (12–19 IIIB)
Epitope ELDRWEKI+ALDKIE
Neutralizing no
Immunogen Vaccine
Vector/Type: viral lysate
Species (Isotype) mouse (IgG)
References Papsidero *et al.* 1989

- 32/5.8.42: Binds to two discontinuous regions, positions 12-19 and 100-105, peptides ELDRWEKI and ALDKIE – inhibited infectivity of cell free virus. Papsidero *et al.* [1989]

No. 4
MAb ID 32/5.8.42
HXB2 Location p17 (12–19)
Author Location p17 (IIIB)
Epitope ELDRWEKI+ALDKIE
Neutralizing no
Immunogen Vaccine
Vector/Type: viral lysate *HIV component:* HIV-1
Species (Isotype) mouse (IgG)
References Papsidero *et al.* 1989

- 32/5.8.42: Inhibited infectivity of cell free virus – bound to two peptides, ELDRWEKI and ALDKIE, at positions 12-19 + 100-105. Papsidero *et al.* [1989]

No. 5
MAb ID HyHIV-1
HXB2 Location p17 (12–29)
Author Location p17 (12–29 JMH1)
Epitope ELDKWEKIRLRPGGKTLY
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG1)
References Ota & Ueda 1998; Liu *et al.* 1995

- HyHIV-1: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. Ota & Ueda [1998]

No. 6
MAb ID HyHIV-2
HXB2 Location p17 (12–29)
Author Location p17 (12–29 JMH1)
Epitope ELDKWEKIRLRPGGKTLY

Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG1)
References Ota & Ueda 1998; Liu *et al.* 1995

- HyHIV-2: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. Ota & Ueda [1998]

No. 7
MAb ID HyHIV-3
HXB2 Location p17 (12–29)
Author Location p17 (12–29 JMH1)
Epitope ELDKWEKIRLRPGGKTLY
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG1)
References Ota & Ueda 1998; Liu *et al.* 1995

- HyHIV-3: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. Ota & Ueda [1998]

No. 8
MAb ID HyHIV-4
HXB2 Location p17 (12–29)
Author Location p17 (12–29 JMH1)
Epitope ELDKWEKIRLRPGGKTLY?
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG1)
References Ota & Ueda 1998; Ota *et al.* 1998; Liu *et al.* 1995

- HyHIV-4: epitope uncertain, based on the best estimate from JMH1 sequence– Ka is 1.8 x 10^7 M-1 for rec p17 – stains the surface of infected cells indicating the antigen is exposed at the cell surface. Ota *et al.* [1998]
- HyHIV-4: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. Ota & Ueda [1998]

No. 9
MAb ID HyHIV-5
HXB2 Location p17 (12–29)
Author Location p17 (12–29 JMH1)
Epitope ELDKWEKIRLRPGGKTLY
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG1)
References Ota & Ueda 1998; Liu *et al.* 1995

- HyHIV-5: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. Ota & Ueda [1998]

No. 10
MAb ID HyHIV-6
HXB2 Location p17 (12–29)
Author Location p17 (12–29 JMH1)
Epitope ELDKWEKIRLRPGGKTLY
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG1)
References Ota & Ueda 1998; Liu *et al.* 1995

- HyHIV-6: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. Ota & Ueda [1998]

No. 11
MAb ID 32/1.24.89
HXB2 Location p17 (17–22)
Author Location p17 (17–22 IIIB)
Epitope EKIRLR
Neutralizing L
Immunogen Vaccine
Vector/Type: viral lysate
Species (Isotype) mouse (IgG)
References Papsidero *et al.* 1989

- 32/1.24.89: Inhibited infectivity of cell free virus. Papsidero *et al.* [1989]

No. 12
MAb ID 3B10
HXB2 Location p17 (19–38)
Author Location p17 (19–38 SIVmac)
Epitope IRLPGGKKKYMLKHVVWAA
Neutralizing no
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Otteken *et al.* 1992

- 3B10: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) , SIVagm, HIV-1, and SIVmnd, demonstrating that the matrix protein of all nine HIV and SIV isolates tested in this study expresses at least one conserved immunogenic epitope recognized serologically. Otteken *et al.* [1992]

No. 13
MAb ID 3E11
HXB2 Location p17 (19–38)
Author Location p17 (19–38 SIVmac)
Epitope IRLPGGKKKYMLKHVVWAA
Neutralizing no
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Nilsen *et al.* 1996; Otteken *et al.* 1992

- 3E11: There is another MAb with this ID that recognizes integrase. Nilsen *et al.* [1996]
- 3E11: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H), SIVagm, HIV-1, and SIVmnd, demonstrating that the matrix protein of all nine HIV and SIV isolates tested in this study expresses at least one highly conserved immunogenic epitope. Otteken *et al.* [1992]

No. 14
MAb ID 8H10
HXB2 Location p17 (30–52)
Author Location p17 (30–52 JMH1)
Epitope KLKHIVWASRELERFAVNPGLLE
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade JMH-1 *HIV component:* p17 Gag *Adjuvant:* BSA
Species (Isotype) mouse (IgM)
References Ota & Ueda 1999; Ota *et al.* 1999

- 8H10: The p17 MAb also can bind to the V3 loop. Ota *et al.* [1999]
- 8H10: Inhibits viral replication of the HIV-1 infected MT-4 cells by decreasing p17 DNA levels in the infected cells, and the effect of growing the 8H10 hybridoma in co-culture with HIV-1 infected MT-4 cells was studied. Ota & Ueda [1999]

No. 15
MAb ID HyHIV-21
HXB2 Location p17 (30–52)
Author Location p17 (30–52 JMH1)
Epitope KLKHIIWASRELERFAVNPGLLE
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG2a)
References Ota *et al.* 1998; Liu *et al.* 1995

- HyHIV-21: epitope uncertain, based on the best estimate from JMH1 sequence – Ka is 3.6 x 10^6 M-1 for rec p17 – stains the surface of infected cells indicating the antigen is exposed at the cell surface –inhibited growth of HIV-1 JMH1 in MT-4 cells when added 24 hours after the initial culture. Ota *et al.* [1998]

No. 16
MAb ID B4f8
HXB2 Location p17 (51–65)
Author Location p17 (51–65)
Epitope LETSEGCRQILGQLQ
Neutralizing no
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) rat (IgG2a)
References Shang *et al.* 1991

- -B4f8: Did not bind live infected cells, only cells that had been made permeable with acetone. Shang *et al.* [1991]

No. 17
MAb ID HyHIV-22
HXB2 Location p17 (52–83)
Author Location p17 (53–87 JMH1)
Epitope ETSEGCRQILGQRQPSLQTGSEELRSLYNTIH
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG1)
References Ota *et al.* 1998; Liu *et al.* 1995

- HyHIV-22: epitope uncertain, based on the best estimate from JMH1 sequence – stains the surface of infected cells indicating the antigen is exposed at the cell surface – Ka is 2.3 x 10^5 M-1 for rec p17. Ota *et al.* [1998]

No. 18
MAb ID 12H-D3b3
HXB2 Location p17 (62–78)
Author Location p17 (62–78)
Epitope GQLQPSLQTGSEELRSL
Neutralizing no
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) rat (IgG2a)
References Shang *et al.* 1991

- 12H-D3b3: Did not bind live infected cells, only cells that had been made permeable with acetone. Shang *et al.* [1991]

No. 19
MAb ID 12G-A8g2
HXB2 Location p17 (86–115)
Author Location p17 (86–115)
Epitope YCVHQRIEIKDTKEALDKIEEEQNKSKKKA
Neutralizing no
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) rat (IgG2a)
References Maksiutov *et al.* 2002; Shang *et al.* 1991

- 12G-A8g2: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein(T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. Maksiutov *et al.* [2002]
- 12G-A8g2: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30. Shang *et al.* [1991]

No. 20
MAb ID 12G-D7h11
HXB2 Location p17 (86–115)
Author Location p17 (86–115)
Epitope YCVHQRIEIKDTKEALDKIEEEQNKSKKKA
Neutralizing no
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) rat (IgG2a)
References Maksiutov *et al.* 2002; Shang *et al.* 1991

- 12G-D7h11: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein (T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. Maksiutov *et al.* [2002]
- 12G-D7h11: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30. Shang *et al.* [1991]

No. 21
MAb ID 12G-H1c7
HXB2 Location p17 (86–115)
Author Location p17 (86–115)
Epitope YCVHQRIEIKDTKEALDKIEEEQNKSKKKA
Neutralizing no
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) rat (IgG)
References Maksiutov *et al.* 2002; Shang *et al.* 1991

- 12G-H1c7: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein (T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. Maksiutov *et al.* [2002]
- 12G-H1c7: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30. Shang *et al.* [1991]

No. 22
MAb ID 12I-D12g2
HXB2 Location p17 (86–115)
Author Location p17 (86–115)
Epitope YCVHQRIEIKDTKEALDKIEEEQNKSKKKA
Neutralizing no
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) rat (IgG2a)
References Maksiutov *et al.* 2002; Shang *et al.* 1991

- 12I-D12g2: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein (T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. Maksiutov *et al.* [2002]
- 12I-D12g2: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30. Shang *et al.* [1991]

No. 23
MAb ID polyclonal
HXB2 Location p17 (86–115)
Author Location p17 (86–115)
Epitope YSVHQRIDVKDTKEALEKIEEEQNKSKKKA
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *HIV component:* p17 Gag *Adjuvant:* Cholera toxin (CT)
Species (Isotype) mouse (IgA)
References Bukawa *et al.* 1995

- Polyclonal secretory IgA antibody raised by oral mucosal immunization is able to neutralize IIIB, SF2, and MN – HIV-1 neutralization may be due to the V3, CD4 or HPG30 component of the multicomponent peptide immunogen. Bukawa *et al.* [1995]

No. 24
MAb ID HyHIV-15
HXB2 Location p17 (87–115)
Author Location p17 (87–115 JMH1)
Epitope SVHQRIDVKDTKEALEKIEEEQNKSKKKA?
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG1)
References Ota *et al.* 1998; Liu *et al.* 1995

- HyHIV-15: epitope uncertain, based on the best estimate from JMH1 sequence – Ka is 1.4 x 10^7 M-1 for rec p17 – stains the surface of infected cells indicating the antigen is exposed at the cell surface – inhibited growth of HIV-1 JMH1 in MT-4 cells when added 24 hours after the initial culture. Ota *et al.* [1998]

No. 25
MAb ID 11H9
HXB2 Location p17 (101–115)
Author Location p17 (101–115 SF2)
Epitope LEKIEEEQNKSKKKA?
Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
Research Contact R. B. Ferns and R. S. Tedder

References Maksiutov *et al.* 2002; Ferns *et al.* 1989; Ferns *et al.* 1987

- 11H9: UK Medical Research Council AIDS reagent: ARP344.
- 11H9: This epitope is similar to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. Maksiutov *et al.* [2002]
- 11H9: Reactive against p18 and p55. Ferns *et al.* [1987]

No. 26
MAb ID 3-H-7 (3H7)
HXB2 Location p17 (113–122)
Author Location p17 (113–122 BH10)
Epitope KKAQQAAADT
Neutralizing L
Immunogen Vaccine
Strain: B clade IIIB
Species (Isotype) mouse (IgG)
References Levin *et al.* 1997; Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b; Niedrig *et al.* 1989

- 3-H-7: Called 3H7 – using a bicistronic vector, an intracellular Fab intrabody, 3H7, can inhibit HIV-1 infection when expressed in the cytoplasm of dividing CD4+ T cells – HXBI-IIB and SI primary isolate virions from 3H7 expressing cells were far less infectious – 3H7 intrabody acts both at the stage of nuclear import and virus particle assembly. Levin *et al.* [1997]
- 3-H-7: No cross-reactivity with HIV-2 ROD or SIV MAC by immunoblot. Niedrig *et al.* [1989]

No. 27
MAb ID C5126
HXB2 Location p17 (113–122)
Author Location p17 (113–122 HXB2)
Epitope KKAQQAAADT
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: viral lysate *HIV component:* HIV-1
Species (Isotype) mouse (IgG1κ)
References Hinkula *et al.* 1990

- C5126: Defined epitope by peptide blocking of binding to native protein – WB reactive with p53 and p17. Hinkula *et al.* [1990]

No. 28
MAb ID 1D9
HXB2 Location p17 (119–132)
Author Location p17 (121–134 SF2)
Epitope AAGTGNSSQVSQNY
Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG2a)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- 1D9: UK Medical Research Council AIDS reagent: ARP316.
- 1D9: Reactive against p18, but not p55. Ferns *et al.* [1987]

No. 29
MAb ID 4C9
HXB2 Location p17 (119–132)
Author Location p18 (121–134 SF2)
Epitope AAGTGNSSQVSQNY
Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG2a)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- 4C9: UK Medical Research Council AIDS reagent: ARP342.
- 4C9: Reactive against p18, but not p55. Ferns *et al.* [1987]

No. 30
MAb ID 4H2B1
HXB2 Location p17 (119–132)
Author Location p17 (121–134 SF2)
Epitope AAGTGNSSQVSQNY
Neutralizing
Immunogen
Species (Isotype) mouse (IgG1)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- 4H2B1: UK Medical Research Council AIDS reagent: ARP315.
- 4H2B1: Reactive against p18 and p55 of multiple isolates. Ferns *et al.* [1987]

No. 31
MAb ID 9G5
HXB2 Location p17 (119–132)
Author Location p17 (121–134 SF2)
Epitope AAGTGNSSQVSQNY
Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgM)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- 9G5: UK Medical Research Council AIDS reagent: ARP343.
- 9G5: Reactive against p18, but not p55. Ferns *et al.* [1987]

No. 32
MAb ID 15-21
HXB2 Location p17 (121–132)
Author Location p17 (121–132 BRU)
Epitope DTGHSSQVSQNY
Neutralizing no
Immunogen Vaccine
Strain: B clade BRU
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b

No. 33
MAb ID 31-11
HXB2 Location p17 (121–132)

Author Location p17 (121–132 BRU)
Epitope DTGHSSQVSQNY
Neutralizing no
Immunogen Vaccine
Strain: B clade BRU
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b

No. 34
MAb ID sc-FV p17
HXB2 Location p17 (121–132)
Author Location p17 (121–132 BRU)
Epitope DTGHSSQVSQNY
Neutralizing L
Immunogen Vaccine
Strain: B clade BRU
Species (Isotype) mouse (IgG1κ)
Ab Type C-term
Research Contact Paul Zhou, NIH, Bethesda, MD, USA
References Tewari *et al.* 1998; Robert-Hebmann *et al.* 1992a

- A single chain Ab (sc-FV) was made from an anti-p17 MAb, and intracellular binding of sc-FV resulted in inhibition of viral replication that was more pronounced when the sc-FV was expressed in the cytoplasm instead of the nucleus. Tewari *et al.* [1998]

IV-C-2 Gag p17-p24 Antibodies

No. 35
MAb ID 3A6
HXB2 Location p17-p24 (122–17)
Author Location p24 (122–149 BH10)
Epitope TGHSSQVSQNYPIVQNIQGQMVHQAISP
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Buchacher *et al.* 1994; Buchacher *et al.* 1992

- 3A6: The reactive peptide spans the p17/p24 border of gag. Buchacher *et al.* [1994]
- 3A6: Human MAbs against HIV generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994]

IV-C-3 Gag p24 Antibodies

No. 36
MAb ID 111/182
HXB2 Location p24 (1–20)
Author Location p24 (134–153 IIIB)
Epitope PIVQNIQGQMVHQAISPRTL
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 111/182: Test specific evidence of cross-reactivity between HIV-1, HIV-2 and SIV MAC. Niedrig *et al.* [1991]

No. 37
MAb ID 112/021
HXB2 Location p24 (1–20)
Author Location p24 (134–153 IIIB)
Epitope PIVQNIQGQMVHQAISPRTL
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 112/021: Test specific evidence of cross-reactivity between HIV-1, HIV-2 and SIV MAC. Niedrig *et al.* [1991]

No. 38
MAb ID 112/047
HXB2 Location p24 (1–20)
Author Location p24 (134–153 IIIB)
Epitope PIVQNIQGQMVHQAISPRTL
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 112/047: Test specific evidence of cross-reactivity between HIV-1, HIV-2 and SIV MAC. Niedrig *et al.* [1991]

No. 39
MAb ID ID8F6
HXB2 Location p24 (11–25)
Author Location p24 (143–157 BRU)
Epitope VHQAISPRTLNAWVK
Neutralizing no
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- ID8F6: UK Medical Research Council AIDS reagent: ARP348.
- ID8F6: Reacted with both p55 and p24 – showed less than 75% homologous inhibition. Ferns *et al.* [1987]

No. 40
MAb ID F5-2
HXB2 Location p24 (14–23)
Author Location p24 (14–23 HXB2)
Epitope AISPRTLNAW
Subtype B
Neutralizing no
Immunogen

Species (Isotype) mouse
References Kusk *et al.* 1992; Kusk *et al.* 1988
- F5-2: In HIV-1 + individuals, antibody to AISPRTLNAW is associated with CD4 T-cell decline. Kusk *et al.* [1988, 1992]

No. 41
MAb ID CB-13/5 (CB-mab-p24/13-15)
HXB2 Location p24 (21–25)
Author Location p24 (152–156)
Epitope NAWVK
Neutralizing no
Immunogen
Species (Isotype) mouse (IgG1κ)
References Glaser & Hausdorf 1996; Kuttner *et al.* 1992; Franke *et al.* 1992; Grunow *et al.* 1990
- CB-13/5: It is not clear whether the MAbs CD-13/5 and CB-mab-p24/13-15 are the same, but from the shared references in the primary articles they seem to be (database note)
- CB-13/5: Epitope described as VHQAISPRTLNAWVK – binding not affected by bound MAb CB-4/1. Glaser & Hausdorf [1996]
- CB-13/5: Inhibits spread of HIV-1 in cell cultures. Franke *et al.* [1992]
- CB-13/5: Called CB-mab-p24/13-15 – the VDJ H and VJ L regions of CB-mab-p24/13-15 were sequenced. Kuttner *et al.* [1992]

No. 42
MAb ID polyclonal
HXB2 Location p24 (44–60)
Author Location p24 (176–192 LAI)
Epitope SEGATPQDLNTMLNTVG
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG)
References Truong *et al.* 1997
- An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. Truong *et al.* [1997]

No. 43
MAb ID 3D3
HXB2 Location p24 (45–50)
Author Location p24 (177–182 LAI)
Epitope EGATPQ
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG2b)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987
- 3D3: UK Medical Research Council AIDS reagent: ARP314.
- 3D3: Most broadly reactive of all the antibodies in this study. Ferns *et al.* [1987]

No. 44
MAb ID CD-4/1 (CB-4/1/1/F6)
HXB2 Location p24 (46–56)
Author Location p24 (182–197)
Epitope GATPQDLNTML
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *HIV component:* p24 Gag
Species (Isotype) mouse (IgG2aκ)
References Ehrhard *et al.* 1996; Glaser & Hausdorf 1996; Hohne *et al.* 1993; Franke *et al.* 1992; Grunow *et al.* 1990
- CD-4/1: Modification of p24 lysine residues by maleic anhydrid increased the affinity of CD-4/1, presumably due to conformational changes exposing a cryptic epitope. Ehrhard *et al.* [1996]
- CD-4/1: Unusual p24-MAb binding kinetics, with biphasic association – probably due to conformational changes in p24, not to p24 dimerization. Glaser & Hausdorf [1996]
- CD-4/1: Affinity of CB-4/1 to native p24 is lower than to peptide or denatured p24 – proposed that the peptide binds in a loop conformation. Hohne *et al.* [1993]
- CD-4/1: Inhibits spread of HIV-1 in cell cultures. Franke *et al.* [1992]

No. 45
MAb ID 15F8C7
HXB2 Location p24 (47–56)
Author Location p24 (183–197)
Epitope ATPQDLNTML
Neutralizing no
Immunogen Vaccine
Vector/Type: purified HIV-1
Species (Isotype) mouse (IgG1)
References Janvier *et al.* 1992; Janvier *et al.* 1990
- 15F8C7: Mapped to aa209-217 through Pepscan method – cross-reacts with HIV-2 Janvier *et al.* [1990] – maps to aa203-217 through EIA pentadecapeptide Janvier *et al.* [1992]. Janvier *et al.* [1990, 1992]

No. 46
MAb ID 111/052
HXB2 Location p24 (51–60)
Author Location p24 (183–192 IIIB)
Epitope DLNTMLNTVG
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag

Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 111/052: Weak cross-reaction with HIV-2 on WB, otherwise not cross-reactive with HIV-2 or SIV MAC. Niedrig *et al.* [1991]

No. 47
MAb ID polyclonal
HXB2 Location p24 (51–82)
Author Location Gag (183–214 LAI)
Epitope DLNTMLNTVGGHQAAMQMLKETINEEAAEWDR
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* p24 Gag *Adjuvant:* QS21
Species (Isotype) human (IgG)
References Pialoux *et al.* 2001

- 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28 (89%), proliferative in 19/28 (79%), and CTL in 13/24 (54%) of testable volunteers – only 4/28 had Ab responses to peptide G1, 4/28 had proliferative responses, and no patient had a CTL response. Pialoux *et al.* [2001]

No. 48
MAb ID 91-5
HXB2 Location p24 (64–75)
Author Location p24 (196–207)
Epitope AAMQMLKETINE
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
References Gorny *et al.* 1998; Robinson *et al.* 1990b; Tyler *et al.* 1990; Gorny *et al.* 1989

- 91-5: NIH AIDS Research and Reference Reagent Program: 1238.
- 91-5: Did not enhance HIV-1 IIIB infection. Robinson *et al.* [1990b]
- 91-5: Synthesized by immortalization of peripheral blood cells with Epstein-Barr virus. Gorny *et al.* [1989]

No. 49
MAb ID 1109/01
HXB2 Location p24 (69–86)
Author Location p24 (201–218 BRU)
Epitope LKETINEEAAEWDRVHPV
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b

No. 50
MAb ID 14D4E11
HXB2 Location p24 (69–86)
Author Location p24 (201–218 BRU)
Epitope LKETINEEAAEWDRVHPV
Neutralizing no
Immunogen Vaccine
Vector/Type: purified HIV-1
Species (Isotype) mouse (IgG1)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b; Janvier *et al.* 1992; Janvier *et al.* 1990

- 14D4E11: Mapped to aa209-217 through Pepscan method (original paper, AAEWDRVHP) – cross-reacts with HIV-2 Janvier *et al.* [1990] and to aa203-217 through EIA pentadecapeptide Janvier *et al.* [1992]. Janvier *et al.* [1990, 1992]

No. 51
MAb ID 1G5C8
HXB2 Location p24 (69–86)
Author Location p24 (201–218 BRU)
Epitope LKETINEEAAEWDRVHPV
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24 Gag
Species (Isotype) mouse (IgG2b)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b; Janvier *et al.* 1992; Janvier *et al.* 1990

- 1G5C8: Mapped to aa209-217 through Pepscan method (original paper, AAEWDRVHP) Janvier *et al.* [1990] and to aa203-217 through EIA pentadecapeptide Janvier *et al.* [1992]. Janvier *et al.* [1990, 1992]

No. 52
MAb ID 47-2
HXB2 Location p24 (69–86)
Author Location p24 (201–218 BRU)
Epitope LKETINEEAAEWDRVHPV
Neutralizing no
Immunogen Vaccine
Strain: B clade BRU
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b

No. 53
MAb ID 714/01
HXB2 Location p24 (69–86)
Author Location p24 (201–218 BRU)
Epitope LKETINEEAAEWDRVHPV
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b

No. 54
MAb ID polyclonal
HXB2 Location p24 (69–86)
Author Location p24 (201–218 LAI)

Epitope LKETINEEAAEWDRVHPV
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse
References Truong *et al.* 1997

- An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. Truong *et al.* [1997]

No. 55
MAb ID 111/073
HXB2 Location p24 (71–81)
Author Location p24 (203–213 IIIB)
Epitope ETINEEAAEWD
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 111/073: cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple assays. Niedrig *et al.* [1991]

No. 56
MAb ID 113/038
HXB2 Location p24 (71–81)
Author Location p24 (203–213 IIIB)
Epitope ETINEEAAEWD
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 113/038: cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple assays. Niedrig *et al.* [1991]

No. 57
MAb ID 1-E-4
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG)
References Niedrig *et al.* 1989

- 1-E-4: One of nine MAbs that bind to this peptide. Niedrig *et al.* [1989]

No. 58
MAb ID 1-E-9
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG)
References Niedrig *et al.* 1989

- 1-E-9: One of nine MAbs that bind to this peptide. Niedrig *et al.* [1989]

No. 59
MAb ID 10-E-7
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 10-E-7: One of nine MAbs that bind to this peptide – cross-reactive with HIV-2 ROD and SIV MAC. Niedrig *et al.* [1989]
- 10-E-7: Cross reactive between HIV-1, HIV-2 and SIV. Niedrig *et al.* [1988]

No. 60
MAb ID 10-G-9
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 10-G-9: One of nine MAbs that bind to this peptide. Niedrig *et al.* [1989]
- 10-G-9: HIV-1 specific. Niedrig *et al.* [1988]

No. 61
MAb ID 11-C-5
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 11-C-5: One of nine MAbs that bind to this peptide. Niedrig *et al.* [1989]
- 11-C-5: HIV-1 specific. Niedrig *et al.* [1988]

No. 62
MAb ID 2-E-4
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG2a)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 2-E-4: One of nine MAbs that bind to this peptide – cross-reactive with HIV-2 ROD. Niedrig *et al.* [1989]
- 2-E-4: Cross reactive between HIV-1, HIV-2 and SIV by ELISA, HIV-1 and HIV-2 by WB. Niedrig *et al.* [1988]

No. 63
MAb ID 2-H-4
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 2-H-4: One of nine MAbs that bind to this peptide – cross-reactive with HIV-2 ROD. Niedrig *et al.* [1989]
- 2-H-4: Cross reactive between HIV-1, HIV-2 and SIV by ELISA, HIV-1 and HIV-2 by WB. Niedrig *et al.* [1988]

No. 64
MAb ID 8-D-2
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG2a)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b; Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 8-D-2: One of nine MAbs that bind to this peptide. Niedrig *et al.* [1989]
- 8-D-2: HIV-1 specific. Niedrig *et al.* [1988]

No. 65
MAb ID 8-G-9
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG)
References Niedrig *et al.* 1989

- 8-G-9: One of nine MAbs that bind to this peptide. Niedrig *et al.* [1989]

No. 66
MAb ID 8-H-7
HXB2 Location p24 (71–85)
Author Location p24 (203–217)
Epitope ETINEEAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG3)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b; Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 8-H-7: One of nine MAbs that bind to this peptide. Niedrig *et al.* [1989]

No. 67
MAb ID C5123
HXB2 Location p24 (71–85)
Author Location p24 (203–217 HXB2)
Epitope ETINEEAAEWDRVHP
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: viral lysate *HIV component:* HIV-1
Species (Isotype) mouse (IgG1κ)
References Hinkula *et al.* 1990

- C5123: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. Hinkula *et al.* [1990]

No. 68
MAb ID 1-B-7
HXB2 Location p24 (76–85)
Author Location p24 (208–217 BH10)
Epitope EAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 1-B-7: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2 and SIV MAC. Niedrig *et al.* [1989]

No. 69
MAb ID 3-B-7
HXB2 Location p24 (76–85)
Author Location p24 (208–217 BH10)
Epitope EAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 3-B-7: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2. Niedrig *et al.* [1989]

No. 70
MAb ID 6-D-12
HXB2 Location p24 (76–85)

Author Location p24 (208–217 BH10)
Epitope EAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 6-D-12: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2. Niedrig *et al.* [1989]

No. 71
MAb ID 6-E-7
HXB2 Location p24 (76–85)
Author Location p24 (208–217 BH10)
Epitope EAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 6-E-7: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2 and SIV MAC. Niedrig *et al.* [1989]

No. 72
MAb ID 8-D-5
HXB2 Location p24 (76–85)
Author Location p24 (208–217 BH10)
Epitope EAAEWDRVHP
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB
Species (Isotype) mouse (IgG)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 8-D-5: Reacts with two overlapping peptides, region of overlap is given – bound only HIV-1. Niedrig *et al.* [1989]

No. 73
MAb ID FF1
HXB2 Location p24 (76–90)
Author Location p24 (208–222 HXB2)
Epitope EAAEWDRVHPVHAGP
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: inactivated HIV
Species (Isotype) mouse (IgG1κ)
References Hinkula *et al.* 1990

- FF1: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. Hinkula *et al.* [1990]

No. 74
MAb ID 113/072
HXB2 Location p24 (81–90)
Author Location p24 (213–222 IIIB)
Epitope DRVHPVHAGP
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 113/072: Weak cross-reaction with HIV-2 on WB, otherwise not cross-reactive with HIV-2 or SIV MAC. Niedrig *et al.* [1991]

No. 75
MAb ID 25.3
HXB2 Location p24 (82–102)
Author Location p24 (82–102)
Epitope RVHPVHAGPIAPGQMREPRGS
Neutralizing no
Immunogen
Species (Isotype) mouse (IgG1κ)
References Momany *et al.* 1996

- 25.3: Crystal structure of the CA protein bound to Fab 25.3 was solved – monomers form 7 alpha-helices arranged in a coiled-coil – Fab binds to a long antigenic peptide that separates the longest helices, with a salt bridge at CA 82 R, and interactions as far away as positions 100 and 102. Momany *et al.* [1996]

No. 76
MAb ID 13-102-100
HXB2 Location p24 (84–94)
Author Location p24 (102–112 IIIB)
Epitope HPVHAGPIAPG
Neutralizing
Immunogen
Species (Isotype) mouse (IgG)
Research Contact Advanced Technologies, Inc., Columbia, MD
References Qian & Tomer 1998; Parker *et al.* 1996

- 13-102-100: Affinity capillary electrophoresis was used to fine map this epitope, and the optimal peptide was defined as VHAGPIAPGIAP – this method uses migration time shifts to probe relative affinities of Abs – the antibody binds to the cyclophilin A binding domain. Qian & Tomer [1998]
- 13-102-100: Binding site (HPVHAGPIAPG) defined by epitope footprinting – first binding p24 to MAb, then allowing proteolytic cleavage to take place to cleave unprotected residues, then performing mass spectrometry to identify protected residues of epitope. Parker *et al.* [1996]

No. 77
MAb ID RL4.72.1
HXB2 Location p24 (87–101)
Author Location p24 (219–233 BRU)
Epitope HAGPIAPGQMREPRG
Neutralizing no
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* D clade NDK *HIV component:* HIV-1
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b; Tatsumi *et al.* 1990

- RL4.72.1: Immunized with inactivated HIV NDK, D clade, reacts with B clade peptide. Robert-Hebmann *et al.* [1992a]

No. 78
MAb ID 406/01
HXB2 Location p24 (101–121)
Author Location p24 (233–253 BRU)
Epitope GSDIAGTTSTLQEQIGWMTNN
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b

No. 79
MAb ID polyclonal
HXB2 Location p24 (101–121)
Author Location p24 (233–253 LAI)
Epitope GSDIAGTTSTLQEQIGWMTNL
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse
References Truong *et al.* 1997

- An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. Truong *et al.* [1997]

No. 80
MAb ID 38:9.6K (38:96K)
HXB2 Location p24 (121–130)
Author Location p24 (253–262 HXB2)
Epitope NPPIPVGEIY
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24-p15 Gag
Species (Isotype) mouse (IgG1κ)
References Hinkula *et al.* 1990

- 38:9.6K: UK Medical Research Council AIDS reagent: ARP365.
- 38:9.6K: Called 38:96K – epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. Hinkula *et al.* [1990]

No. 81
MAb ID EB1A9
HXB2 Location p24 (121–135)
Author Location p24 (253–267 LAI)
Epitope NPPIPVGEIYKRWII
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- EB1A9: UK Medical Research Council AIDS reagent: ARP345.
- EB1A9: Reacted with both p55 and p24 – showed less than 75% homologous inhibition. Ferns *et al.* [1987]

No. 82
MAb ID polyclonal
HXB2 Location p24 (121–152)
Author Location Gag (253–284 LAI)
Epitope NPPIPVGEIYKRWIILGLNKIVRMYSPTSILD
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* p24 Gag *Adjuvant:* QS21
Species (Isotype) human (IgG)
References Pialoux *et al.* 2001

- 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28 (89%), proliferative in 19/28 (79%), and CTL in 13/24 (54%) of testable volunteers – 25/28 had Ab responses to peptide G2, 14/28 had proliferative responses, and CTL responses were detected. Pialoux *et al.* [2001]

No. 83
MAb ID 30:3E5
HXB2 Location p24 (141–170)
Author Location p24 (273–302 HXB2)
Epitope IVRMYSPTSILDIRQGPKEPFRDYVDRFYK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24-p15 Gag
Species (Isotype) mouse (IgG1λ)
Research Contact B. Wahren
References Hinkula *et al.* 1990

- 30:3E5: UK Medical Research Council AIDS reagent: ARP367.
- 30:3E5: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. Hinkula *et al.* [1990]

No. 84
MAb ID EF7
HXB2 Location p24 (141–170)
Author Location p24 (273–302 HXB2)
Epitope IVRMYSPTSILDIRQGPKEPFRDYVDRFYK
Subtype B

Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24-p15 Gag
Species (Isotype) mouse (IgG1κ)
References Lundin *et al.* 1996; Hinkula *et al.* 1990

- EF7: UK Medical Research Council AIDS reagent: ARP366.
- EF7: Included as a control. Lundin *et al.* [1996]
- EF7: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53. Hinkula *et al.* [1990]

No. 85
MAb ID LH-104-E
HXB2 Location p24 (143–148)
Author Location p24 (275–280 BRU)
Epitope RMYSPT
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BRU
Species (Isotype) mouse (IgG1κ)
References Haaheim *et al.* 1991

- LH-104-E: UK Medical Research Council AIDS reagent: ARP319.
- LH-104-E: Reacts with both p24 and p55. Haaheim *et al.* [1991]

No. 86
MAb ID 1B2C12
HXB2 Location p24 (149–154)
Author Location p24 (273–292 IIIB)
Epitope SILDIR
Neutralizing no
Immunogen Vaccine
Vector/Type: purified HIV-1
Species (Isotype) mouse (IgG1)
References Janvier *et al.* 1992; Janvier *et al.* 1990

- 1B2C12: Reacts with HIV-1 and HIV-2– mapped to aa281-286 through Pepscan method Janvier *et al.* [1990], and to aa273-292 through EIA pentadecapeptide method Janvier *et al.* [1992]. Janvier *et al.* [1990, 1992]

No. 87
MAb ID LH-104-K
HXB2 Location p24 (149–154)
Author Location p24 (281–286 BRU)
Epitope SILDIR
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BRU
Species (Isotype) mouse (IgG1κ)
References Haaheim *et al.* 1991

- LH-104-K: UK Medical Research Council AIDS reagent: ARP322.
- LH-104-K: Binds exclusively with p24 (not p55) Haaheim *et al.* [1991]

No. 88
MAb ID LH-104-A
HXB2 Location p24 (152–157)
Author Location p24 (BRU)
Epitope DIRQGP+QGVGGP
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1κ)
References Haaheim *et al.* 1991

- LH-104-A: UK Medical Research Council AIDS reagent: ARP307.
- LF-104-A: A 104 amino acid peptide was used to immunize mice – hexapeptide scans revealed two reactive p24 peptides – cross-competition studies indicated the region 270-286. Haaheim *et al.* [1991]

No. 89
MAb ID 1.17.3
HXB2 Location p24 (152–172)
Author Location p24 (152–172 SIVmac)
Epitope CVKQGPKEPFQSYVDRFYKSL
Neutralizing no
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Otteken *et al.* 1992

- 1.17.3: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) and HIV-2smmH4, but not SIVagmTYO-1, HIV-1 IIIB or SIVmnd. Otteken *et al.* [1992]

No. 90
MAb ID 1A7
HXB2 Location p24 (152–172)
Author Location p24 (152–172 SIVmac)
Epitope CVKQGPKEPFQSYVDRFYKSL
Neutralizing no
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Otteken *et al.* 1992

- 1A7: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) and HIV-2smmH4, but not SIVagmTYO-1, HIV-1 IIIB or SIVmnd. Otteken *et al.* [1992]

No. 91
MAb ID 1F6
HXB2 Location p24 (152–172)
Author Location p24 (152–172 SIVmac)
Epitope CVKQGPKEPFQSYVDRFYKSL
Neutralizing no
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Otteken *et al.* 1992

- 1F6: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) and HIV-2smmH4, but not SIVagmTYO-1, HIV-1 IIIB or SIVmnd. Otteken *et al.* [1992]

No. 92

MAb ID 23A5G4
HXB2 Location p24 (153–172)
Author Location p24 (285–304 IIIB)
Epitope IRQGPKEPFRDYVDRFYKTL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Janvier *et al.* 1996; Janvier *et al.* 1992; Janvier *et al.* 1990

- 23A5G4: A few sera which were able to bind the linear sequence 178-192, but not sequence 288-302 in an indirect peptide ELISA inhibited the binding of 23A5G4 to the native p24. Janvier *et al.* [1996]
- 23A5G4: Mapped to aa209-217 through Pepscan method Janvier *et al.* [1990] and to aa285-304 through EIA pentadecapeptide method Janvier *et al.* [1992]. Janvier *et al.* [1990, 1992]

No. 93
MAb ID 23A5G5
HXB2 Location p24 (153–172)
Author Location p24 (285–304 BRU)
Epitope IRQGPKEPFRDYVDRFYKTL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b

No. 94
MAb ID 3D10G6
HXB2 Location p24 (153–172)
Author Location p24 (285–304 IIIB)
Epitope IRQGPKEPFRDYVDRFYKTL
Neutralizing no
Immunogen Vaccine
Vector/Type: purified HIV-1
Species (Isotype) mouse (IgG1)
References Janvier *et al.* 1992; Janvier *et al.* 1990

- 3D10G6: Epitope cross-reacts with HIV-1 and HIV-2– mapped to aa260-267 through Pepscan method Janvier *et al.* [1990] and to aa285-304 through EIA pentadecapeptide method. Janvier *et al.* [1990, 1992]

No. 95
MAb ID polyclonal
HXB2 Location p24 (153–172)
Author Location p24 (285–304 LAI)
Epitope IRQGPKEPFRDYVDRFYKTL
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse
References Truong *et al.* 1997

- An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. Truong *et al.* [1997]

No. 96
MAb ID F5-4
HXB2 Location p24 (153–175)
Author Location p24 (153–174 HXB2)
Epitope IRQGPKEPFRDYVDRFYKTLRAE
Subtype B
Neutralizing no
Immunogen
Species (Isotype) mouse
References Kusk *et al.* 1992; Kusk *et al.* 1988

- F5-4: Binds to a location in the most hydrophilic region of p24. Kusk *et al.* [1988, 1992]

No. 97
MAb ID MO9.42.2
HXB2 Location p24 (153–178)
Author Location p24 (285–310 BRU)
Epitope IRQGPKEPFRDYVDRFYKTLRAEQAS
Neutralizing no
Immunogen Vaccine
Vector/Type: virus *Strain:* HIV-2 ROD *HIV component:* HIV-1
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b

- MO9.42.2: Reacts with HIV-1s, HIV-2s, and SIVs in rec protein ELISA. Robert-Hebmann *et al.* [1992b]

No. 98
MAb ID MO9.50.2
HXB2 Location p24 (153–178)
Author Location p24 (285–310 BRU)
Epitope IRQGPKEPFRDYVDRFYKTLRAEQAS
Neutralizing no
Immunogen Vaccine
Strain: HIV-2 ROD
Species (Isotype) mouse (IgG)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b

- MO9.50.2: Reacts with HIV-1s, HIV-2s, and SIVs in rec protein ELISA. Robert-Hebmann *et al.* [1992b]

No. 99
MAb ID V10
HXB2 Location p24 (155–169)
Author Location p24 (289–303 IIIB)
Epitope QGPKEPFRDYVDRFY
Neutralizing no

Immunogen virus
Species (Isotype) mouse
References Matsuo *et al.* 1992

- V10: Reacts with HIV-1 and SIV AGM analogous peptides. Matsuo *et al.* [1992]

No. 100
MAb ID V107
HXB2 Location p24 (155–177)
Author Location p24 (289–311 IIIB)
Epitope QGPKEPFRDYVDRFYKTLRAEQA
Neutralizing no
Immunogen virus
Species (Isotype) mouse
References Matsuo *et al.* 1992

- V107: Reacts with FIV, HIV-1 and SIV AGM analogous peptides. Matsuo *et al.* [1992]

No. 101
MAb ID LH-104-C
HXB2 Location p24 (156–161)
Author Location p24 (BRU)
Epitope GPKEPF+QGVGGP
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *HIV component:* p24 Gag
Species (Isotype) mouse (IgG3κ)
References Haaheim *et al.* 1991

- LH-104-C: UK Medical Research Council AIDS reagent: ARP309.
- LF-104-C: A 104 amino acid peptide was used to immunize mice – hexapeptide scans revealed two reactive p24 peptides – cross-competition studies indicated the region 351-373. Haaheim *et al.* [1991]

No. 102
MAb ID 12-B-4
HXB2 Location p24 (161–170)
Author Location p24 (293–302 IIIB)
Epitope FRDYVDRFYK
Neutralizing no
Immunogen Vaccine
Strain: B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1989; Niedrig *et al.* 1988

- 12-B-4: Epitope is defined as the overlap between two HIV-1 reactive peptides – cross-reacts with HIV-2 ROD and SIV MAC. Niedrig *et al.* [1988, 1989]

No. 103
MAb ID C5122
HXB2 Location p24 (161–170)
Author Location p24 (293–302 HXB2)
Epitope FRDYVDRFYK
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: viral lysate *HIV component:* HIV-1
Species (Isotype) mouse (IgG1κ)
References Hinkula *et al.* 1990

- C5122: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. Hinkula *et al.* [1990]

No. 104
MAb ID 9A4C4
HXB2 Location p24 (170–188)
Author Location p24 (303–317 IIIB)
Epitope KTLRAEQASQEVKNWMTET
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Robert-Hebmann *et al.* 1992a; Robert-Hebmann *et al.* 1992b; Janvier *et al.* 1992; Janvier *et al.* 1990

- 9A4C4: Mapped to aa260-267 through Pepscan method Janvier *et al.* [1990] – and to aa303-317 through EIA pentadecapeptide method Janvier *et al.* [1992]. Janvier *et al.* [1990, 1992]

No. 105
MAb ID 11C10B10
HXB2 Location p24 (171–185)
Author Location p24 (303–317 IIIB)
Epitope TLRAEQASQEVKNWM
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Janvier *et al.* 1992; Janvier *et al.* 1990

- 11C10B10: Mapped to aa260-267 through Pepscan method Janvier *et al.* [1990] and to aa303-317 through EIA pentadecapeptide method Janvier *et al.* [1992]. Janvier *et al.* [1990, 1992]

No. 106
MAb ID 11D11F2
HXB2 Location p24 (171–185)
Author Location p24 (303–317 IIIB)
Epitope TLRAEQASQEVKNWM
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Janvier *et al.* 1992; Janvier *et al.* 1990

- 11D11F2: Mapped to aa260-267 through Pepscan method Janvier *et al.* [1990] and to aa303-317 through EIA pentadecapeptide method Janvier *et al.* [1992]. Janvier *et al.* [1990, 1992]

No. 107
MAb ID CD12B4
HXB2 Location p24 (171–185)
Author Location p24 (303–317 LAI)
Epitope TLRAEQASQEVKNWM
Subtype B

Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- CD12B4: UK Medical Research Council AIDS reagent: ARP346.
- CD12B4: Reacted with both p55 and p24 – strain-specific binding. Ferns *et al.* [1987]

No. 108
MAb ID BE3
HXB2 Location p24 (176–190)
Author Location p24 (308–322 HXB2)
Epitope QASQEVKNWMTETLL
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24-p15 Gag
Species (Isotype) mouse (IgG1κ)
Research Contact B. Wahren
References Hinkula *et al.* 1990

- BE3: UK Medical Research Council AIDS reagent: ARP368.
- BE3: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. Hinkula *et al.* [1990]

No. 109
MAb ID L14
HXB2 Location p24 (176–190)
Author Location p24 (308–322 HXB2)
Epitope QASQEVKNWMTETLL
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24-p15 Gag
Species (Isotype) mouse (IgG1κ)
Research Contact B. Wahren
References Hinkula *et al.* 1990

- L14: UK Medical Research Council AIDS reagent: ARP369.
- L14: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. Hinkula *et al.* [1990]

No. 110
MAb ID 108/03
HXB2 Location p24 (181–190)
Author Location p24 (313–322 IIIB)
Epitope VKNWMTETLL
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 108/03: Cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple tests. Niedrig *et al.* [1991]

No. 111
MAb ID 110/015
HXB2 Location p24 (181–190)
Author Location p24 (313–322 IIIB)
Epitope VKNWMTETLL
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 110/015: Cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple tests. Niedrig *et al.* [1991]

No. 112
MAb ID 32:32K
HXB2 Location p24 (199–222)
Author Location p24 (331–354 HXB2)
Epitope KTILKALGPAATLEEMMTACQGVG
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24-p15 Gag
Species (Isotype) mouse (IgG1λ)
References Hinkula *et al.* 1990

- 32:32K: UK Medical Research Council AIDS reagent: ARP368.
- 32:32K: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. Hinkula *et al.* [1990]

No. 113
MAb ID C5200
HXB2 Location p24 (199–222)
Author Location p24 (331–354 HXB2)
Epitope KTILKALGPAATLEEMMTACQGVG
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: viral lysate
Species (Isotype) mouse (IgG1κ)
References Hinkula *et al.* 1990

- C5200: Epitope defined by peptide blocking of binding to native protein. Hinkula *et al.* [1990]

No. 114
MAb ID FH2
HXB2 Location p24 (201–215)
Author Location p24 (333–347 HXB2)
Epitope ILKALGPAATLEEMM
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24-p15 Gag
Species (Isotype) mouse (IgG1κ)
References Hinkula *et al.* 1990

- FH2: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. Hinkula *et al.* [1990]

No. 115
MAb ID 13B5
HXB2 Location p24 (205–214)
Author Location p24 (205–213)
Epitope LGPAATLEEM
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24 Gag
Species (Isotype) mouse
Ab Type C-term
Research Contact bioMerieux
References Berthet-Colominas *et al.* 1999

- 13B5: Fab which was bound to p24 capsid for crystallization and study of p24's structure. Berthet-Colominas *et al.* [1999]

No. 116
MAb ID 106/01
HXB2 Location p24 (211–230)
Author Location p24 (343–362 IIIB)
Epitope LEEMMTACQGVGGPGHKARV
Neutralizing no
Immunogen Vaccine
Vector/Type: beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1991

- 106/01: Cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple tests. Niedrig *et al.* [1991]

No. 117
MAb ID LH-104-B
HXB2 Location p24 (225–230)
Author Location p24 (357–362 BRU)
Epitope GHKARV
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BRU
Species (Isotype) mouse (IgG1κ)
References Haaheim *et al.* 1991

- LH-104-B: UK Medical Research Council AIDS reagent: ARP308.
- LH-104-B: Binds exclusively with p55 (not p24), in contrast to LH-104-I. Haaheim *et al.* [1991]

No. 118
MAb ID LH-104-I
HXB2 Location p24 (226–231)
Author Location p24 (358–363 BRU)
Epitope HKARVL
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BRU
Species (Isotype) mouse (IgG1κ)
References Haaheim *et al.* 1991

- LH-104-I: UK Medical Research Council AIDS reagent: ARP321.
- LH-104-I: Binds exclusively with p24 (not p55), in contrast to LH-104-B. Haaheim *et al.* [1991]

IV-C-4 Gag p24-p2p7p1p6 Antibodies

No. 119
MAb ID LH-104-G
HXB2 Location p24-p2p7p1p6 (231–5)
Author Location p24 (363–368 BRU)
Epitope LAEAMS
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BRU
Species (Isotype) mouse (IgG1κ)
References Haaheim *et al.* 1991

- LH-104-G: This epitope overlaps the p24-p2 cleavage site, database note.
- LH-104-G: UK Medical Research Council AIDS reagent: ARP320.
- LH-104-G: Reacts with both p24 and p55, in contrast to LH-104-I. Haaheim *et al.* [1991]

IV-C-5 Gag p2p7p1p6 Antibodies

No. 120
MAb ID i5B11
HXB2 Location p2p7p1p6 (19–28)
Author Location p7 (5–14)
Epitope NFRNQRKIVK
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) rat (IgG2a)
References Tanchou *et al.* 1995; Tanchou *et al.* 1994; Otake *et al.* 1994

- i5B11: i5B11 and 15B11 may be two names for the same MAb.
- i5B11: MAb reacts with NCp7, NCp15, and partially inhibits NCp7-tRNA interaction. Tanchou *et al.* [1995]
- i5B11: Epitope mapped by ELISA and BIAcore – inhibits NCp7 primer tRNA binding. Tanchou *et al.* [1994]

No. 121
MAb ID EC6
HXB2 Location p2p7p1p6 (45–54)
Author Location p15 (408–417 HXB2)
Epitope PRKKGCWKCG
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24-p15 Gag
Species (Isotype) mouse (IgG2aκ)
References Hinkula *et al.* 1990

- EC6: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53. Hinkula *et al.* [1990]

No. 122
MAb ID M12
HXB2 Location p2p7p1p6 (45–54)
Author Location p15 (408–417 HXB2)
Epitope PRKKGCWKCG
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p24-p15 Gag
Species (Isotype) mouse (IgG1κ)
References Hinkula *et al.* 1990

- M12: There is a p15 and a gp120 MAb both called M12.
- M12: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53. Hinkula *et al.* [1990]

No. 123
MAb ID DG8
HXB2 Location p2p7p1p6 (66–81)
Author Location p7 (52–67)
Epitope RQANFLGKIWPSYKGR
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse
References Tanchou *et al.* 1995

- DG8: Binds proximal to the second zinc-finger, inhibits NCp7-tRNA interaction. Tanchou *et al.* [1995]

No. 124
MAb ID EB5
HXB2 Location p2p7p1p6 (66–81)
Author Location p7 (52–67)
Epitope RQANFLGKIWPSYKGR
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse
References Tanchou *et al.* 1995

- EB5: Binds proximal to the second zinc-finger – mutation at position 59 (Lys to Ser) results in 10-fold reduction in reactivity. Tanchou *et al.* [1995]

No. 125
MAb ID HH3
HXB2 Location p2p7p1p6 (66–81)
Author Location p7 (52–67)
Epitope RQANFLGKIWPSYKGR
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG2b)
References Tanchou *et al.* 1995; Tanchou *et al.* 1994

- HH3: Binds proximal to the second zinc-finger. Tanchou *et al.* [1995]
- HH3: Epitopes mapped by ELISA and BIAcore – does not inhibit NCp7 primer tRNA binding. Tanchou *et al.* [1994]

No. 126
MAb ID AD2
HXB2 Location p2p7p1p6 (78–86)
Author Location p7 (64–72)
Epitope YKGRPGNFL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- AD2: Binds at C term of NCp7. Tanchou *et al.* [1995]

No. 127
MAb ID CA5
HXB2 Location p2p7p1p6 (78–86)
Author Location p7 (64–72)
Epitope YKGRPGNFL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- CA5: Binds at C term of NCp7. Tanchou *et al.* [1995]

No. 128
MAb ID DF3
HXB2 Location p2p7p1p6 (78–86)
Author Location p7 (64–72)
Epitope YKGRPGNFL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- DF3: Binds at C term of NCp7. Tanchou *et al.* [1995]

No. 129
MAb ID EC3
HXB2 Location p2p7p1p6 (78–86)
Author Location p7 (64–72)
Epitope YKGRPGNFL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- EC3: Binds at C term of NCp7. Tanchou *et al.* [1995]

No. 130
MAb ID FC12
HXB2 Location p2p7p1p6 (78–86)

Author Location p7 (64–72)
Epitope YKGRPGNFL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- FC12: Binds at C term of NCp7, reacts with NCp15, inhibits NCp7-tRNA interaction. Tanchou *et al.* [1995]

No. 131
MAb ID GE4
HXB2 Location p2p7p1p6 (78–86)
Author Location p7 (64–72)
Epitope YKGRPGNFL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- GE4: Binds at C term of NCp7. Tanchou *et al.* [1995]

No. 132
MAb ID JB7
HXB2 Location p2p7p1p6 (78–86)
Author Location p7 (64–72)
Epitope YKGRPGNFL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- JB7: Binds at C term of NCp7. Tanchou *et al.* [1995]

No. 133
MAb ID JF11
HXB2 Location p2p7p1p6 (78–86)
Author Location p7 (64–72)
Epitope YKGRPGNFL
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG1)
References Tanchou *et al.* 1995; Tanchou *et al.* 1994

- JF11: Binds at C term of NCp7. Tanchou *et al.* [1995]
- JF11: Epitopes mapped by ELISA and BIAcore – does not inhibit NCp7 primer tRNA binding. Tanchou *et al.* [1994]

IV-C-6 Gag Antibodies

No. 134
MAb ID 16/4/2
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: DNA with CMV promotor, DNA with CMV/MCK hybrid promotor, DNA with MCK promotor
Species (Isotype)
References Bojak *et al.* 2002a

- 16/4/2: The ability of three different promoters to induce Gag specific immune responses was compared. The cytomegaliovirus (CMV) early gene promoter, which allows constitutive expression in different cells of host tissue, the tissue specific muscle creatine kinase (MCK) promoter, which may be restricted to differentiated, multinucleated myofibers and so safer, and a hybrid MCK/CMV promoter – intramuscular immunization of BALB/c mice utilizing the MCK promoter in combination with a codon optimized gag gene generated humoral (IgG1 (Th1) and IgG2a (Th2)) and CTL immune responses against HIV-1 Gag, however, the quantified immune parameters were clearly reduced as compared to CMV promotor-driven Gag expression. Bojak *et al.* [2002a]

No. 135
MAb ID 183-H12-5C
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen
Species (Isotype) mouse (IgG1)
Research Contact Bruce Chesebro and Kathy Wehrly, Rocky Mountain Laboratories, Hamilton, Montana
References Wehrly & Chesebro 1997; Toohey *et al.* 1995; Chesebro *et al.* 1992

- 183-H12-5C: NIH AIDS Research and Reference Reagent Program: 3537.
- 183-H12-5C: Cross-reacts with HIV1 and HIV-2 p24, and SIV p27. Wehrly & Chesebro [1997]
- 183-H12-5C: Used as antigen capture reagent for p24 ELISA. Chesebro *et al.* [1992]; Toohey *et al.* [1995]

No. 136
MAb ID 241-D
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen
Species (Isotype) human (IgG1λ)
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Robinson *et al.* 1991; Tyler *et al.* 1990; Gorny *et al.* 1989

- 241-D: MH AIDS Research and Reference Reagent program: 1244.
- 241-D: An antibody by this name is available in the NIH AIDS Research and Reference Reagent Program, and they refer to the papers Gorny *et al.* [1989]; Tyler *et al.* [1990]; Robinson *et al.* [1991], but no p24 MAb by this name is discussed in these papers. Gorny *et al.* [1989]; Robinson *et al.* [1991]; Tyler *et al.* [1990]

No. 137
MAb ID 2A6
HXB2 Location Gag
Author Location p17
Epitope
Neutralizing
Immunogen
Species (Isotype)
Research Contact A. O. Arthur, Frederick Cancer Research and Development Center, Frederick, MD
References Pincus *et al.* 1998

- 2A6: Part of a panel of 17 MAbs used as controls testing for the dual specificity of MAb G11H3 for both p17 and mycoplasma. Pincus *et al.* [1998]

No. 138
MAb ID 5E2.A3k
HXB2 Location Gag
Author Location p24 (1–158 SF2)
Epitope
Neutralizing no
Immunogen
Species (Isotype) mouse (IgG1)
Research Contact Biodesign International, Kennebunk, Maine, USA
References Hochleitner *et al.* 2000a

- 5E2.A3k: The Ab binding site was studied with epitope excision (protein is bound in native conformation to immobilized MAb, then digested with proteolytic enzymes) and extraction (protein is digested then allowed to react with Ab), followed by mass spectroscopy, as well as lysine modification – the epitope is discontinuous, but involves the highly conserved N-term proline, and the antibody recognizes SIVs and HIV-2 as well as HIV-1 p24. Hochleitner *et al.* [2000a]

No. 139
MAb ID 71-31
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen
Species (Isotype) human (IgG1λ)
References Bandres *et al.* 1998; Gorny *et al.* 1998; Gorny *et al.* 1997; Spear *et al.* 1993; Robinson *et al.* 1991; Robinson *et al.* 1990b; Gorny *et al.* 1989

- 71-31: NIH AIDS Research and Reference Reagent Program: 530.
- 71-31: Included as a negative control in studies that demonstrate that CXCR4 can bind to gp120 in the absence of CD4-gp120 interactions, and that this binding can be enhanced by Env deglycosylation. Bandres *et al.* [1998]
- 71-31: Did not mediate deposition of complement component C3 on HIV infected cells. Spear *et al.* [1993]
- 71-31: No enhancing or neutralizing activity. Robinson *et al.* [1991]
- 71-31: Did not enhance HIV-1 IIIB infection. Robinson *et al.* [1990b]

No. 140
MAb ID 91-6
HXB2 Location Gag
Author Location p24 (121–240 IIIB)
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
References Robinson *et al.* 1990b; Gorny *et al.* 1989

- 91-6: NIH AIDS Research and Reference Reagent Program: 1239.
- 91-6: No enhancing activity for HIV-1 IIIB. Robinson *et al.* [1990b]

No. 141
MAb ID 98-4.3
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
References Robinson *et al.* 1991

- 98-4.3: No enhancing or neutralizing activity. Robinson *et al.* [1991]

No. 142
MAb ID 98-4.9
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) mouse (IgG3λ)
References Gorny *et al.* 1989

No. 143
MAb ID AC2
HXB2 Location Gag
Author Location p7
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- AC2: Binds NCp7 independent of Zn fingers, does not react with NCp15. Tanchou *et al.* [1995]

No. 144
MAb ID BC1071
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) mouse
Research Contact Aalto BioReagents
References Schonning *et al.* 1999

- BC1071: The stoichiometry of MAb neutralization was tested and MAb BC1071 was used in this study for virion quantification. Schonning *et al.* [1999]

No. 145
MAb ID BE10
HXB2 Location Gag
Author Location p7
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- BE10: Binding NCp7 requires Zn fingers, does not react with NCp15, inhibits NCp7-tRNA interaction. Tanchou *et al.* [1995]

No. 146
MAb ID CD9
HXB2 Location Gag
Author Location p7
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- CD9: Binds NCp7 independent of Zn fingers, does not react with NCp15. Tanchou *et al.* [1995]

No. 147
MAb ID CH9B2
HXB2 Location Gag
Author Location p17
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- CH9B2: UK Medical Research Council AIDS reagent: ARP349.
- CH9B2: Reactive against p18 and p55. Ferns *et al.* [1987]

No. 148
MAb ID ED8
HXB2 Location Gag
Author Location p7
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p7 Gag
Species (Isotype) mouse (IgG)
References Tanchou *et al.* 1995

- ED8: Binds NCp7 independent of Zn fingers, does not react with NCp15. Tanchou *et al.* [1995]

No. 149
MAb ID EH12E1
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- EH12E1: UK Medical Research Council AIDS reagent: ARP313.
- EH12E1: Reacted with p55 and p24 in WB. Ferns *et al.* [1987]

No. 150
MAb ID G11G1
HXB2 Location Gag
Author Location p17
Epitope
Neutralizing
Immunogen
Species (Isotype) rat
References Pincus *et al.* 1996; Shang *et al.* 1991

- G11G1: Immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but only if the antigen was expressed at the cell surface – ricin-G11G1 did not mediate cell killing. Pincus *et al.* [1996]

No. 151
MAb ID G11H3
HXB2 Location Gag
Author Location p17
Epitope
Neutralizing
Immunogen
Species (Isotype)
References Pincus *et al.* 1998; Shang *et al.* 1991

- G11H3: This MAb is cross-reactive between p17 and mycoplasma – this antibody binds strain specifically to the variable lipoprotein (Vlp) F of M. hyorhinis, in the region of the carboxy-terminal repeat CGGSTPTPEQGNNQGGSTPTPEQGNSQVSK – the p17 epitope is discontinuous, but p17 and Vlp F share the tetrapeptide SQVS. Pincus *et al.* [1998]

No. 152
MAb ID HyHIV-19

HXB2 Location Gag
Author Location p17 (JMH1)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* p17 Gag
Species (Isotype) mouse (IgG1)
References Ota *et al.* 1998; Liu *et al.* 1995

- HyHIV-19: Does not react with p17 peptides – Ka is 3.7 x 10^6 M-1 for rec p17 – inhibited growth of HIV-1 JMH1 in MT-4 cells when added 24 hours after the initial culture. Ota *et al.* [1998]

No. 153
MAb ID IE8G2
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
Research Contact R. B. Ferns and R. S. Tedder
References Ferns *et al.* 1989; Ferns *et al.* 1987

- IE8G2: UK Medical Research Council AIDS reagent: ARP347.
- IE8G2: Reacted with both p55 and p24 – broadly reactive – showed less than 75% homologous inhibition. Ferns *et al.* [1987]

No. 154
MAb ID V7-8
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) mouse (IgG3κ)
References Montefiori *et al.* 1991; Robinson *et al.* 1990b

- V7-8: NIH AIDS Research and Reference Reagent Program: 381.
- V7-8: Reacted with HIV-1IIIB, RF, and MN. Montefiori *et al.* [1991]
- V7-8: Did not enhance HIV-1 IIIB infection. Robinson *et al.* [1990b]

No. 155
MAb ID anti-p24
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *HIV component:* Gag, gp120, Nef, Pol
Species (Isotype) mouse (IgG)
Research Contact Intracel Co
References Buonaguro *et al.* 2001

- anti-p24: HIV-1 pr55 gag-based virus-like particles (VLP) carrying Nef and Pol open reading frames, as well as gp120 of the clade A isolate 94UG018, were created using a Baculovirus expression system to package additional ORFS into the VLP – anti-V3 and anti-p24 Abs were used to assess the expression levels and Gag and gp120-TM were found to be expressed at comparable levels on the VLP. Buonaguro *et al.* [2001]

No. 156
MAb ID human sera
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Binley *et al.* 1997b

- Retention of anti-Env antibodies and loss of anti-Gag antibodies during progression was studied, and suggested to be the result of the loss of T-cell help and the unique ability of Env to stimulate B cells even in a backdrop of declining CD4 cells, because of the ability of Env to bind to the CD4 molecule. Binley *et al.* [1997b]

No. 157
MAb ID polyclonal
HXB2 Location Gag
Author Location Gag (LAI)
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: DNA prime with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18
Species (Isotype) mouse
References Billaut-Mulot *et al.* 2001

- DNA vaccinated BALB/c mice primed and boosted with a multiepitopic vaccine with IL18 showed lymphoproliferative and CTL responses – co-administration of IL18 increased T-cell responses but decreased anti-HIV Ab levels. Billaut-Mulot *et al.* [2001]

No. 158
MAb ID polyclonal
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: gp120 depleted whole killed virus *Strain:* AG recombinant HZ321 *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA), CpG immunostimulatory sequence (ISS)
Species (Isotype) rat
References Moss *et al.* 2000

- Different HIV strains were used for different regions: subtype A env, subtype G gag.

- Lewis rats co-immunized with HIV-1 antigen in Freund's and with immunostimulatory sequences CpG stimulated increased IFNγ expressing CD4+ and CD8+ T cells and anti-p24 antibodies relative to antigen in Freund's without CpG. Moss *et al.* [2000]

No. 159
MAb ID polyclonal
HXB2 Location Gag
Author Location p24 (SF2)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF2 *HIV component:* gp120, p24 Gag *Adjuvant:* MF59, PLG
Species (Isotype) mouse
References O'Hagan *et al.* 2000

- Microparticles were used as an adjuvant for entrapped HIV-1 gp120 and induced strong serum IgG responses in mice – polylactide co-glycolide polymer (PLG) microparticles in combination with MF-59 had the highest Ab response and also induced p24 specific CTL. O'Hagan *et al.* [2000]

No. 160
MAb ID polyclonal
HXB2 Location Gag
Author Location Gag (SF2)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA, protein *Strain:* B clade SF2 *HIV component:* Gag *Adjuvant:* aluminum phosphate, MF59, PLG
Species (Isotype) macaque, guinea pig, mouse
References O'Hagan *et al.* 2001

- DNA vaccines of codon-optimized Env and Gag genes driven by CMV promotors absorbed on to PLG microparticles were more effective than naked DNA at eliciting strong Ab responses (more rapid, higher titer, more stable), comparable to gp120 in MF-59. O'Hagan *et al.* [2001]

No. 161
MAb ID polyclonal
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade *HIV component:* p24 Gag
Species (Isotype) rabbit (IgG)
References Gupta *et al.* 2001

- Gag p24 is the mostly widely used HIV protein for serological based diagnostic kits — phage display libraries of HIV-1 p24 identified 2 epitope-rich regions: 70% of the clones that were identified using immunized rabbit sera had DNA fragments from the N-terminal region spanning 150–240 of Gag, and 30% from the carboxy-terminal region of p24 containing amino acids 310–360 — subtype B and C comparisons were made. Gupta *et al.* [2001]

No. 162
MAb ID polyclonal
HXB2 Location Gag
Author Location p55
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* CD4BS, Gag, V3
Species (Isotype) mouse
References Truong *et al.* 1996

- Antibodies raised against recombinant anti-p55 virus-like particles with the p24 region 196-226 deleted, bearing inserts of either the V3 or the CD4BS regions of gp120 were studied – no neutralizing responses, weak Env and strong Gag responses were elicited – the major homology region (MHR) and proximal sequences was found to be required for capsid assembly. Truong *et al.* [1996]

No. 163
MAb ID polyclonal
HXB2 Location Gag
Author Location p24 (LAI)
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: peptide, virion, baculovirus, E. Coli recombinant protein *Strain:* B clade LAI *HIV component:* p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA), Incomplete Freund's Adjuvant (IFA)
Species (Isotype) rabbit (IgG)
References Devito *et al.* 2000c

- To compare vaccine strategies, rabbits were immunized with virion HIV-1/Lai, baculovirus recombinant p24, E. coli recombinant p24-15, and p24-derived peptides – the rabbit immunized with peptides had the broadest linear epitope responses – the capture ELISA method using anti-p24 IgG preparations was shown to capture isolates from HIV-1 subtypes or clades A to G – only immunization with virion HIV-1/Lai and baculovirus recombinant p24 developed IgG that was capable of efficiently capturing HIV-1 p24 in ELISA producing Abs able to recognise native configurations. Devito *et al.* [2000c]

No. 164
MAb ID polyclonal
HXB2 Location Gag
Author Location
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA *Adjuvant:* CpG immunostimulatory sequence (ISS), phosphorothioate oligodeoxynucleotides (ODNs)
Species (Isotype) mouse

References Deml *et al.* 2001

- Immunization mice with a codon-optimized Gag was compared with a non-optimized Rev dependent Gag expression vector – Gag expression was at higher levels and Rev independent with the codon-optimized Gag, and i.m. immunization gave a stronger Th1-driven humoral and cellular immune response – intradermal immunization with either Gag DNA induced a Th2 response and no CTL. Deml *et al.* [2001]

No. 165
MAb ID polyclonal
HXB2 Location Gag
Author Location
Epitope
Neutralizing yes
Immunogen HIV-1 infection
Species (Isotype) human
References Montefiori *et al.* 2001

- In 7/9 patients in whom HAART was initiated during early seroconversion, NAbs to autologous strains were not found immediately following treatment interuption after 1-3 years, and Env and Gag Abs were low or undetected by ELISA indicating, that early HAART suppresses the normal antibody response to HIV-1, presumably by limiting the concentration of viral antigens needed to drive B-cell maturation – in 3 patients with a viral rebound autologous NAbs rapidly appeared and correlated with spontaneous down-regulation of viremia – prolonged control of viremia after stopping treatment persisted in the absence of detectable NAbs, suggesting that cellular immune responses alone can control viremia under certain circumstances – these results support the notion that virus-specific B-cell priming, combined with CD8+ CTL induction, may be beneficial for HIV-1 vaccines that aim to suppress viremia in the absence of complete protection to prevent disease and reduce the rate of virus transmission. Montefiori *et al.* [2001]

No. 166
MAb ID polyclonal
HXB2 Location Gag
Author Location
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* Env, Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG)
References Lebedev *et al.* 2000

- Virus-like particles (VLPs) in the form of spherical particles with yeast dsRNA enveloped in a polysaccharide matrix carrying the protein TBI, that contains fragments of HIV Env and Gag, were used to immunize BALB/c mice and induced specific Abs against HIV-1 as measured by ELISA with TBI. Lebedev *et al.* [2000]

No. 167
MAb ID polyclonal
HXB2 Location Gag
Author Location
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: DNA with CMV promotor, DNA with CMV/MCK hybrid promotor, DNA with MCK promotor
Species (Isotype) mouse (IgG1, IgG2a)
References Bojak *et al.* 2002a

- The ability of three different promoters to induce Gag specific immune responses was compared. The cytomegaliovirus (CMV) early gene promoter, which allows constitutive expression in different cells of host tissue, the tissue specific muscle creatine kinase (MCK) promoter, which may be restricted to differentiated, multinucleated myofibers and so safer, and a hybrid MCK/CMV promoter – intramuscular immunization of BALB/c mice utilizing the MCK promoter in combination with a codon optimized gag gene generated humoral (IgG1 (Th1) and IgG2a (Th2)) and CTL immune responses against HIV-1 Gag, however, the quantified immune parameters were clearly reduced as compared to CMV promotor-driven Gag expression. Bojak *et al.* [2002a]

No. 168
MAb ID polyclonal
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human
References Meles *et al.* 2002

- Indeterminant WB in Ethiopians: of 12,124 specimens blood specimens from Ethiopia, 1,437 (11.9%) were HIV-1-positive for antibody, and 91 (0.8%) gave equivocal results, most often due to p24 reactivity – subsequent testing confirmed many of the indeterminants were HIV-negative – the American Red Cross diagnostic criteria was more accurate than CDC or WHO, which would have given some false positive results. Meles *et al.* [2002]

No. 169
MAb ID polyclonal
HXB2 Location Gag
Author Location p24
Epitope
Subtype A
Neutralizing yes
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* A clade UG5.94UG018 *HIV component:* Gag, gp120
Species (Isotype) mouse
References Buonaguro *et al.* 2002
Country Uganda
Keywords inter-clade comparisons

- BALB/c mice were immunized with VLPs carrying a subtype A gp120. Humoral immune responses directed against B-clade derived Gag (p24) peptides or gp120-Env V3 loop peptide were readily induced following a multi-dose immunization with VLP particles presenting a gp120 molecule from a HIV-1 isolate of

clade A. VLP-immunized mice showed autologous and heterologous (against B-clade HIV-1 IIIB strain) neutralization activity. Proliferative responses and CTL were also observed. Buonaguro *et al.* [2002] (**inter-clade comparisons**)

No. 170
MAb ID polyclonal
HXB2 Location Gag
Author Location Gag
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Gag
Species (Isotype) mouse (IgG1)
References Bojak *et al.* 2002b
Keywords Th1

- Balb/c mice vaccinated by syngag, a DNA plasmid expressing HIV-1 Gag modified for human/mammalian codon usage, gave stronger and longer lasting immune responses than wild type gag. Gag-specific antibody and cellular immune responses were both increased, with a clear T-helper 1 polarization. There was a better IgG1/IgG2 response to intramuscular (i.m.) as compared to subcutaneous (s.c.) vaccination. Bojak *et al.* [2002b] (**Th1**)

No. 171
MAb ID polyclonal
HXB2 Location Gag
Author Location Gag
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA, protein, virus-like particle (VLP), PLG microparticle *Adjuvant:* E. coli heat labile enterotoxin
Species (Isotype) macaque
References Otten *et al.* 2003

- This study evaluates different vaccine technologies that avoid live vectors including plasmid DNA, recombinant p55Gag protein or gag-pol administered by polylactide coglycolide (PLG) microparticles, LTK63 as adjuvant, VLP, and plasmid DNA. 4/4 macaques primed with Gag-PLG and LTK63 showed strong antibody responses after the fourth immunization at week six. The best CTL responses were found for gag DNA, the best Th and Ab were obtained using Gag protein on PLG microparticles; Gag DNA priming with a PLG-protein boost gave high level CTL, Th and Ab responses. Otten *et al.* [2003]

No. 172
MAb ID polyclonal HIVIG
HXB2 Location Gag
Author Location p24
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Nichols *et al.* 2002

- NYBC-HIVIG derived from patients with high NAb titers and NABI-HIVIG derived from patients with high anti-p24 Ab titers were compared in neutralizing assay against a panel of six primary isolates—both could neutralize all isolates tested but the NYBC-HIVIG dose required for 50% neutralization was of 3.2 fold lower, showing that the source plasmas influence the effective concentration of NAb present in HIVIG. Nichols *et al.* [2002]

IV-C-7 Protease Antibodies

No. 173
MAb ID 1696
HXB2 Location Protease (1–7)
Author Location Protease (1–7 BH10)
Epitope PQIYLWQ
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Protease
Species (Isotype) mouse (IgG)
Ab Type N-term
References Lescar *et al.* 2003; Rezacova *et al.* 2002; Rezacova *et al.* 2001; Lescar *et al.* 1999
Keywords review, structure

- 1696: Study compares the crystal structure of the scFv-1696 in the non-complexed form compared to the complexed Fab-1696 and the Ag-bound scFv-1696 structures. Changes in the three conformational tertiary structures of CDR-H3 as well as in the different relative orientations of the light-chain variable domains of the different structures were observed, demonstrating plasticity in the antibody binding site. Lescar *et al.* [2003] (**structure**)
- 1696: Review of the implications of antibody structure and antigen peptide binding for the mechanisms of inhibition of protease activity by two MABs with different binding sites in protease. Rezacova *et al.* [2002] (**review**, **structure**)
- 1696: The crystal structure of the single chain Fv fragment of 1696 bound to a cross-reactive peptide (PQITLWQRR) was obtained. This sturcture suggests that 1696 inhibits portease activity by favoring dissociation of the active homodimer. Rezacova *et al.* [2001] (**structure**)
- 1696: MAb binds to HIV-1 and HIV-2, putative epitopes are PQIYLWQ and PQFSLWK respectively – Pro1 is critical, QIYLWQR residues 2-8, does not compete - MAb disrupts catalytic activity – crystal structure of the ligand-free Fab at 3 A resolution reveals a deep cavity lined by acidic and hydrophobic residues – the binding region is located within the region required for dimerization and the Fab structure could serve as a basis for drug design targeting this region. Lescar *et al.* [1999] (**structure**)

No. 174
MAb ID 10E7
HXB2 Location Protease (36–46)
Author Location Protease (38–45 HXB2)
Epitope MSLPGRWKPKM
Subtype B

Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Protease
Species (Isotype) hamster (IgG)
References Bjorling *et al.* 1992; Croix *et al.* 1993

- 10E7: Immunodominant region of protease in Armenian hamster (but only weakly reactive in people, see: Bjorling *et al.* [1992]) – peptide MSLPGRWKP blocks protease binding Croix *et al.* [1993]. Bjorling *et al.* [1992]; Croix *et al.* [1993]

No. 175
MAb ID F11.2.32
HXB2 Location Protease (36–46)
Author Location Protease (36–46 BH10)
Epitope MSLPGRWKPKM
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10 *HIV component:* Protease
Species (Isotype) mouse (IgG1κ)
Ab Type flap region
References Rezacova *et al.* 2002; Lescar *et al.* 1999; Lescar *et al.* 1997; Lescar *et al.* 1996
Keywords review, structure

- F11.2.32: Review of the implications of antibody structure and antigen peptide binding for the mechanisms of inhibition of protease activity by two MABs with different binding sites in protease. Rezacova *et al.* [2002] (**review**, **structure**)
- F11.2.32: Crystal strucutre of a Fab peptide complex was obtained. Distortion may occur in the flap region of the protein, important for regulating access of substrate to the catalytic site. Lescar *et al.* [1999] (**structure**)
- F11.2.32: Binding leads to significant inhibition in proteolytic activity – crystal structure of Fab-peptide was determined to 2.2 A resolution – bound peptide shows no structural similarity to the corresponding segment in native protease suggesting binding may distort protein structure. Lescar *et al.* [1997] (**structure**)

No. 176
MAb ID 13E1
HXB2 Location Protease (38–45)
Author Location Protease (38–45 HXB2)
Epitope LPGRWKPK
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Protease
Species (Isotype) hamster (IgG)
References Croix *et al.* 1993

- 13E1: Binds to MSLPGRWKPKM with sightly higher affinity. Croix *et al.* [1993]

No. 177
MAb ID 8B11
HXB2 Location Protease (38–45)
Author Location Protease (38–45 HXB2)
Epitope LPGRWKPK
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Protease
Species (Isotype) hamster (IgG)
References Croix *et al.* 1993

- 8B11: Binds to MSLPGRWKPKM with sightly higher affinity. Croix *et al.* [1993]

No. 178
MAb ID 8C10
HXB2 Location Protease (38–45)
Author Location Protease (38–45 HXB2)
Epitope LPGRWKPK
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Protease
Species (Isotype) hamster (IgG)
References Croix *et al.* 1993

- 8C10: Binds to MSLPGRWKPKM with sightly higher affinity. Croix *et al.* [1993]

No. 179
MAb ID 8G5
HXB2 Location Protease (38–45)
Author Location Protease (38–45 HXB2)
Epitope LPGRWKPK
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Protease
Species (Isotype) hamster (IgG)
References Croix *et al.* 1993

- 8G5: Binds to MSLPGRWKPKM with sightly higher affinity. Croix *et al.* [1993]

IV-C-8 RT Antibodies

No. 180
MAb ID 1E8
HXB2 Location RT (65–73)
Author Location RT (65–73)
Epitope KKDSTKWRK
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* RT *Adjuvant:* nitrocellulose
Species (Isotype) mouse (IgG1)
References Gu *et al.* 1996; Wu *et al.* 1993

- 1E8: Significantly inhibits DNA polymerase activity of RT by hindering binding of dNTPs – additive or synergistic RT inhibition with nevirapine and delavirdine. Gu *et al.* [1996]
- 1E8: Inhibits RT activity, binding site overlaps with two AZT resistance mutations. Wu *et al.* [1993]

No. 181
MAb ID polyclonal
HXB2 Location RT (249–263)
Author Location RT (249–263)
Epitope KDSWTVNDIQKLVGK
Neutralizing
Immunogen Vaccine, in vitro stimulation or selection *Vector/Type:* peptide presented on icosahedral protein scaffold *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (Isotype) human (IgG)
Ab Type C2
References Domingo *et al.* 2003
Keywords vaccine antigen design

- A virus-like protein scaffold, called E2DISP, derived from pyruvate dehydrogenase multienzyme from Bacillus stearothermophilus has been engineered to display 60 copies of one or more epitopes on a single molecule. An E2DISP scaffold which displayed pep23, a 15-residue B and T helper HIV-1 RT epitope elicited a pep23-specific T-helper response *in vitro*. The E2DISP scaffold displaying peptide RT2, which is a CTL HIV-1 RT epitope, was able to elicit a CD8+ T cell response *in vitro* and in a vaccinated HLA-A2 transgenic mouse. Thus the E2DISP scaffold allows cell-entry and access to both the class I and class II processing pathways. The Th response in vaccinated mice supported Pep23-specific IgG responses. Domingo *et al.* [2003] (**vaccine antigen design**)

No. 182
MAb ID 1.152 B3
HXB2 Location RT (294–302)
Author Location RT (294–302)
Epitope PLTEEAELE
Neutralizing no
Immunogen Vaccine *Vector/Type:* protein *HIV component:* RT
Species (Isotype) mouse (IgG1)
References Orvell *et al.* 1991

- 1.152 B3: Weakly positive by immunofluorescence – binding inhibits RT enzymatic activity. Orvell *et al.* [1991]

No. 183
MAb ID 1.158 E2
HXB2 Location RT (294–302)
Author Location RT (294–302)
Epitope PLTEEAELE
Neutralizing no
Immunogen Vaccine *Vector/Type:* protein *HIV component:* RT
Species (Isotype) mouse (IgG1)
References Orvell *et al.* 1991

- 1.158 E2: Negative by immunofluorescence – binding inhibits RT enzymatic activity. Orvell *et al.* [1991]

No. 184
MAb ID 31D6
HXB2 Location RT (294–318)
Author Location RT (294–319)
Epitope PLTEEAELELAENREILKEPVHGVY
Neutralizing no
Immunogen Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT
Species (Isotype) mouse (IgG1)
References Szilvay *et al.* 1992

- 31D6: Strong inhibitor of RT, > 50% inhibition. Szilvay *et al.* [1992]

No. 185
MAb ID 31G8
HXB2 Location RT (294–318)
Author Location RT (294–319)
Epitope PLTEEAELELAENREILKEPVHGVY
Neutralizing no
Immunogen Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT
Species (Isotype) mouse (IgG1)
References Szilvay *et al.* 1992

- 31G8: Weak inhibitor of RT, reactive by immunofluorescence. Szilvay *et al.* [1992]

No. 186
MAb ID 32E7
HXB2 Location RT (294–318)
Author Location RT (294–319)
Epitope PLTEEAELELAENREILKEPVHGVY
Neutralizing no
Immunogen Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT
Species (Isotype) mouse (IgG1)
References Szilvay *et al.* 1992

- 32E7: Weak inhibitor of RT, reactive by immunofluorescence. Szilvay *et al.* [1992]

No. 187
MAb ID 33D5
HXB2 Location RT (294–318)
Author Location RT (294–319)
Epitope PLTEEAELELAENREILKEPVHGVY
Neutralizing no
Immunogen Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT
Species (Isotype) mouse (IgG1)
References Szilvay *et al.* 1992

- 33D5: Weak inhibitor of RT, reactive by immunofluorescence. Szilvay *et al.* [1992]

No. 188
MAb ID 5B2
HXB2 Location RT (294–318)
Author Location RT (294–319)
Epitope PLTEEAELELAENREILKEPVHGVY
Neutralizing no
Immunogen Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT
Species (Isotype) mouse (IgG1)

References Szilvay *et al.* 1992

- 5B2: UK Medical Research Council AIDS reagent: ARP3018.
- 5B2: There is an RT specific Ab Szilvay *et al.* [1992] and a gp41 specific Ab Tian *et al.* [2001] both called 5B2. Szilvay *et al.* [1992]
- 5B2: Weak inhibitor of RT, reactive by immunofluorescence. Szilvay *et al.* [1992]

No. 189
MAb ID polyclonal
HXB2 Location RT (295–304)
Author Location RT (295–304 PV22)
Epitope LTEEAELELA
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Grimison & Laurence 1995

No. 190
MAb ID 1.153 G10
HXB2 Location RT (350–354)
Author Location RT (350–354)
Epitope KTGKY
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* RT
Species (Isotype) mouse (IgG1)
References Orvell *et al.* 1991

No. 191
MAb ID RTMAb8
HXB2 Location RT (376–383)
Author Location RT (532–539)
Epitope TTESIVIW
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* RT
Species (Isotype) mouse (IgG)
References Ferns *et al.* 1991; Tisdale *et al.* 1988

No. 192
MAb ID 1D4A3
HXB2 Location RT (384–387)
Author Location RT (540–543)
Epitope GKIP
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* RT
Species (Isotype) mouse (IgG)
References Ferns *et al.* 1991

No. 193
MAb ID RT6H
HXB2 Location RT (384–387)
Author Location RT (540–543)
Epitope GKIP
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* RT
Species (Isotype) mouse (IgG)
References Ferns *et al.* 1991

No. 194
MAb ID 1.160 B3
HXB2 Location RT (442–450)
Author Location RT (442–450)
Epitope VDGAANRET
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* RT
Species (Isotype) mouse (IgG1)
References Orvell *et al.* 1991

No. 195
MAb ID polyclonal
HXB2 Location RT (521–531)
Author Location RT (521–531 PV22)
Epitope IIEQLIKKEKV
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Grimison & Laurence 1995

No. 196
MAb ID C2003
HXB2 Location RT (536–549)
Author Location RT (703–716 BH10)
Epitope VPAHKGIGGNEQVD
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10
Species (Isotype) rabbit (IgG)
References DeVico *et al.* 1991

- C2003: Inhibits polymerase activity from a variety of retroviruses – RT protected from inhibition by preincubation with template primer. DeVico *et al.* [1991]

No. 197
MAb ID 5B11
HXB2 Location RT
Author Location RT (BH-10)
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Research Contact Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal
References Herschhorn *et al.* 2003
Keywords antibody generation, antibody sequence, variable domain, immunotherapy

- 5B11: One of five human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. Herschhorn *et al.* [2003] (**antibody generation**, **immunotherapy**, **antibody sequence, variable domain**)

No. 198
MAb ID 6B10
HXB2 Location RT
Author Location RT (BH-10)
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Research Contact Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal
References Herschhorn *et al.* 2003
Keywords antibody generation, antibody sequence, variable domain

- 6B10:One of five human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (DDDP and RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. In contrast, 6B10 seemed to enhance DDDP activity and did not effect RDDP. Herschhorn *et al.* [2003] (**antibody generation**, **antibody sequence, variable domain**)

No. 199
MAb ID 6E9
HXB2 Location RT
Author Location RT (BH-10)
Epitope
Subtype B
Neutralizing
Immunogen in vitro stimulation or selection
Species (Isotype) human
Research Contact Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal
References Herschhorn *et al.* 2003
Keywords antibody generation, antibody sequence, variable domain, immunotherapy

- 6E9: One of five human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. Herschhorn *et al.* [2003] (**antibody generation**, **immunotherapy**, **antibody sequence, variable domain**)

No. 200
MAb ID E-4
HXB2 Location RT
Author Location RT (BH-10)
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Research Contact Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal
References Herschhorn *et al.* 2003
Keywords antibody generation, antibody sequence, variable domain

- E-4:One of five human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. In contrast, E-4 seemed to enhance RDDP. Herschhorn *et al.* [2003] (**antibody generation**, **antibody sequence, variable domain**)

No. 201
MAb ID 6B9
HXB2 Location RT
Author Location RT (155–250)
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade HXB2 *HIV component:* RT
Species (Isotype) mouse (IgG)
Ab Type palm domain
References Ohba *et al.* 2001; Chiba *et al.* 1997; Chiba *et al.* 1996

- 6B9: In contrast to MAb 7C4, which binds to the thumb region of RT, 6B9 binds to the palm subdomain and does not inhibit RT activity. Chiba *et al.* [1996]

No. 202
MAb ID 5F
HXB2 Location RT
Author Location RT (252–335)
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade HXB2 *HIV component:* RT
Species (Isotype) mouse
Ab Type thumb domain
References Ohba *et al.* 2001

- 5F: BALB/c mice were vaccinated with vaccinia carrying RT and a phage display library was produced and panned with RT – Fabs 5F and 5G were cloned, both recognizing an immunodominant neutralizing RT epitope in the region of the template primer-binding site in the thumb domain also recognized by MAb 7C4 – sequencing revealed the heavy chains and light chains of 7C4, 5G and 7C4 are related. Ohba *et al.* [2001]

No. 203
MAb ID 5G
HXB2 Location RT
Author Location RT (252–335)
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade HXB2 *HIV component:* RT
Species (Isotype) mouse
Ab Type thumb domain

References Ohba *et al.* 2001

- 5G: BALB/c mice were vaccinated with vaccinia carrying RT and a phage display library was produced and panned with RT – Fabs 5F and 5G were cloned, both recognizing an immunodominant neutralizing RT epitope in the region of the template primer-binding site in the thumb domain also recognized by MAb 7C4 – sequencing revealed the heavy chains and light chains of 7C4, 5G and 7C4 are related. Ohba *et al.* [2001]

No. 204
MAb ID 7C4
HXB2 Location RT
Author Location RT (252–335)
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade HXB2 *HIV component:* RT
Species (Isotype) mouse (IgG2a)
Ab Type thumb domain
References Ohba *et al.* 2001; Chiba *et al.* 1997; Chiba *et al.* 1996

- 7C4: Fabs 5F and 5G both recognize the same immunodominant neutralizing RT epitope in the region of the template primer-binding site in the thumb domain recognized by MAb 7C4 – sequencing revealed the heavy chains and light chains of 7C4, 5G and 7C4 are related. Ohba *et al.* [2001]
- 7C4: 7C4 inhibits RT from HIV-1 strains IIIB, Bru, and IMS-1 but not HIV-2 strains GH-1 and LAV-2, SIV MAC, nor SIV MND. Chiba *et al.* [1997]
- 7C4: 7C4 was produced from a hybridoma cell line derived from a BALB/c mouse repeatedly immunized with RT in a vaccinia construct, and was found to inhibit RT through binding to the template primer-binding site, a possible target for RT inhibitors. Chiba *et al.* [1996]

IV-C-9 Integrase Antibodies

No. 205
MAb ID 1C4
HXB2 Location Integrase (1–16)
Author Location Integrase (1–16 HXB2)
Epitope FLDGIDKAQDEHEKYH
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996; Haugan *et al.* 1995

- 1C4: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]
- 1C4: MAb interferes with integrase binding to DNA. Haugan *et al.* [1995]

No. 206
MAb ID 2C11
HXB2 Location Integrase (1–16)
Author Location Integrase (1–16 HXB2)
Epitope FLDGIDKAQDEHEKYH
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996

- 2C11: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]

No. 207
MAb ID 2E3
HXB2 Location Integrase (1–16)
Author Location Integrase (1–16 HXB2)
Epitope FLDGIDKAQDEHEKYH
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Ovod *et al.* 1992; Nilsen *et al.* 1996

- 2E3: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]
- 2E3: There are two MAbs called 2E3 – the other one binds to Nef. Ovod *et al.* [1992]

No. 208
MAb ID 3E11
HXB2 Location Integrase (1–16)
Author Location Integrase (1–16 HXB2)
Epitope FLDGIDKAQDEHEKYH
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996; Otteken *et al.* 1992

- 3E11: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]
- 3E11: There is another MAb with this ID that recognizes p17. Otteken *et al.* [1992]

- 3E11: Recognized an epitope present on HIV-2/SIVmac, SIVagm, HIV-1, and SIVmnd. Otteken *et al.* [1992]

No. 209
MAb ID 3F9
HXB2 Location Integrase (1–16)
Author Location Integrase (1–16 HXB2)
Epitope FLDGIDKAQDEHEKYH
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2
HIV component: Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996

- 3F9: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]

No. 210
MAb ID 5F8
HXB2 Location Integrase (1–16)
Author Location Integrase (1–16 HXB2)
Epitope FLDGIDKAQDEHEKYH
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2
HIV component: Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996; Haugan *et al.* 1995

- 5F8: There is another MAb with this ID that recognizes and unknown protein in HIV.
- 5F8: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]
- 5F8: MAb interferes with integrase binding to DNA. Haugan *et al.* [1995]

No. 211
MAb ID 6G5
HXB2 Location Integrase (1–16)
Author Location Integrase (1–16 HXB2)
Epitope FLDGIDKAQDEHEKYH
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2
HIV component: Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996

- 6G5: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]

No. 212
MAb ID 7B6
HXB2 Location Integrase (1–16)
Author Location Integrase (1–16 HXB2)
Epitope FLDGIDKAQDEHEKYH
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2
HIV component: Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996

- 7B6: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]

No. 213
MAb ID 7C6
HXB2 Location Integrase (1–16)
Author Location Integrase (1–16 HXB2)
Epitope FLDGIDKAQDEHEKYH
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2
HIV component: Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996

- 7C6: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]

No. 214
MAb ID 6C5
HXB2 Location Integrase (17–38)
Author Location Integrase (17–38 HXB2)
Epitope SNWRAMASDFNLPPVVAKEIVA
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2
HIV component: Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996; Haugan *et al.* 1995

- 6C5: This MAb inhibits end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]

- 6C5: MAb interferes with integrase binding to DNA. Haugan *et al.* [1995]

No. 215
MAb ID 8G4
HXB2 Location Integrase (22–31)
Author Location Integrase (12–42 HXB2)
Epitope MASDFNLPPV+GYIEAEVIPAETGQETAYFI?
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
References Nilsen *et al.* 1996; Haugan *et al.* 1995

- 8G4: This MAb reacted strongly with peptides IN(12-31) and IN(22-42), and less strongly with peptide IN(82-101) – it did not react with a deletion mutant of positions 17-38 – this MAb inhibits end processing and DNA joining, but had little effect on integration activities. Nilsen *et al.* [1996]
- 8G4: MAb interferes with integrase binding to DNA. Haugan *et al.* [1995]

No. 216
MAb ID 17 (mAb17)
HXB2 Location Integrase (25–35)
Author Location Integrase (25–35)
Epitope DFNLPPVVAKE
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG1)
References Yi *et al.* 2000; Levy-Mintz *et al.* 1996; Bizub-Bender *et al.* 1994

- 17: Epitope mapped to helix-turn-helix motif in the N-term domain of Integrase, positions 25-35 – Zn binding stabilizes the Integrase-mAb17 complex – both MAb and Fab form of mAb17 inhibit Integrase activity – epitope region likely to be involved in protein-protein interaction. Yi *et al.* [2000]
- 17: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. Levy-Mintz *et al.* [1996]
- 17: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 14 and 17 form a competition group. Bizub-Bender *et al.* [1994]

No. 217
MAb ID 4D6
HXB2 Location Integrase (42–55)
Author Location Integrase (42–55 HXB2)
Epitope KCQLKGEAMHGQVD
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
Ab Type N-term
References Nilsen *et al.* 1996; Haugan *et al.* 1995

- 4D6: This MAb inhibits end processing and DNA joining, and reduces reintegration activity. Nilsen *et al.* [1996]
- 4D6: MAb interferes with integrase binding to DNA. Haugan *et al.* [1995]

No. 218
MAb ID 7-16 (7-19)
HXB2 Location Integrase (50–159)
Author Location Integrase (50–159 HXB2)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int
Species (Isotype) mouse (IgG2b)
Ab Type Integrase catalytic core
Research Contact Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan
References Ishikawa *et al.* 1999

- 7-16: Binds to the central catalytic domain – the paper seems to sometimes call this antibody 7-16, sometimes 7-19, a possible typo. Ishikawa *et al.* [1999]

No. 219
MAb ID 4F6
HXB2 Location Integrase (56–102)
Author Location Integrase (56–102 HXB2)
Epitope CSPGIWQLDCTHLEGKVILVAVHVASGYIEAE-VIPAETGQETAYFLL
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
Ab Type Integrase catalytic core
References Nilsen *et al.* 1996; Haugan *et al.* 1995

- 4F6: MAb binding had minimal effects on IN *in vitro* activities. Nilsen *et al.* [1996]
- 4F6: MAb interferes with integrase binding to DNA. Haugan *et al.* [1995]

No. 220
MAb ID anti-K159
HXB2 Location Integrase (151–163)
Author Location Integrase (163–175)
Epitope VESMNKELKKIIG
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* Int
Species (Isotype) rabbit (IgG)
References Maksiutov *et al.* 2002; Maroun *et al.* 1999

- anti-K159: This epitope is similar to a fragment of the human protein Apoptosis regulator BCL-W (KIAA0271), ESVNKEMEPLVGQV. Maksiutov *et al.* [2002]
- anti-K159: Both the peptide K159, SQGVVESMNKELKKIIGQVRDQAEHLKTA, and the Abs raised against this peptide inhibit Integrase activity – K159 was found to fulfill condition of minimal number of helical heptads to achieve the formation of a stable coiled-coil structure – Integrase is proposed to function as a dimer interacting in this region. Maroun *et al.* [1999]

No. 221
MAb ID 5D9
HXB2 Location Integrase (186–250)
Author Location Integrase (186–250 HXB2)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
Ab Type Integrase DNA binding domain
References Nilsen *et al.* 1996; Haugan *et al.* 1995

- 5D9: MAb binding had minimal effects on IN *in vitro* activities. Nilsen *et al.* [1996]
- 5D9: While C-term and N-term anti-Integrase MAbs interfere with Integrase-DNA binding, 5D9 which binds more centrally, does not. Haugan *et al.* [1995]

No. 222
MAb ID 8-6
HXB2 Location Integrase (211–227)
Author Location Integrase (211–227 HXB2)
Epitope KELQKQITKIQNFRVYY
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int
Species (Isotype) mouse (IgG1)
Research Contact Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan
References Ishikawa *et al.* 1999

- 8-6: Antibody binds proximal to the DNA binding region. Ishikawa *et al.* [1999]

No. 223
MAb ID 19 (2-19, scAb2-19)
HXB2 Location Integrase (228–236)
Author Location Integrase (228–236 LAI)
Epitope RDSRNPLWK
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG1)
References Kitamura *et al.* 1999; Levy-Mintz *et al.* 1996; Bizub-Bender *et al.* 1994

- 19: Called 2-19, scAb2-19 is a single-chain Ab made from MAb 2-19 –acts intra-cellularly to block infection at low MOI by binding to integrase – scAb interfered with the folding of Gag-Pol polyprotein, the Ab did not affect viral production in LAI transfected cells, but the virus produced was less infectious – authors suggest that the epitope may be conformational. Kitamura *et al.* [1999]
- 19: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – 19 has a low binding affinity. Bizub-Bender *et al.* [1994]

No. 224
MAb ID 2-19
HXB2 Location Integrase (228–236)
Author Location Integrase (228–236 HXB2)
Epitope RDSRNPLWK
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int
Species (Isotype) mouse (IgG2b)
Ab Type Integrase DNA binding domain
Research Contact Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan
References Ishikawa *et al.* 1999

- 2-19: MAb inhibits RT-Integrase interaction, and the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity. Ishikawa *et al.* [1999]

No. 225
MAb ID 8-22
HXB2 Location Integrase (237–252)
Author Location Integrase (237–252 HXB2)
Epitope GPAKLLWKGEGAVVIQ
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int
Species (Isotype) mouse (IgG1)
Ab Type Integrase DNA binding domain
Research Contact Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan
References Ishikawa *et al.* 1999

- 8-22: MAb inhibits the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity. Ishikawa *et al.* [1999]

No. 226
MAb ID 4-20
HXB2 Location Integrase (253–261)
Author Location Integrase (253–261 HXB2)

Epitope DNSDIKVVP
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int
Species (Isotype) mouse (IgG1)
Ab Type Integrase DNA binding domain
Research Contact Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan
References Ishikawa *et al.* 1999

- 4-20: Inhibits the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity. Ishikawa *et al.* [1999]

No. 227
MAb ID 6-19
HXB2 Location Integrase (262–270)
Author Location Integrase (261–270 HXB2)
Epitope RRKAKIIRD
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int
Species (Isotype) mouse (IgG2b)
Ab Type Integrase DNA binding domain
Research Contact Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan
References Ishikawa *et al.* 1999

- 6-19: Inhibits the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity. Ishikawa *et al.* [1999]

No. 228
MAb ID 7C3
HXB2 Location Integrase (262–271)
Author Location Integrase (262–271 HXB2)
Epitope RRKAKIIRDY
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
References Nilsen *et al.* 1996; Haugan *et al.* 1995

- 7C3: A set of three MAbs recognize an epitope in this region, 7C3, 7F11, and 8E5 – all three HIV-1 MAbs cross-react with HIV-2 IN – these MAbs inhibit end-processing, DNA joining and reintegration, and had little effect on disintegration. Nilsen *et al.* [1996]
- 7C3: MAb interferes with integrase binding to DNA. Haugan *et al.* [1995]

No. 229
MAb ID 7F11
HXB2 Location Integrase (262–271)
Author Location Integrase (262–271 HXB2)
Epitope RRKAKIIRDY
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
References Lasky *et al.* 1987; Nilsen *et al.* 1996

- 7F11: A set of three MAbs recognize an epitope in this region, 7C3, 7F11, and 8E5 – all three HIV-1 MAbs cross-react with HIV-2 IN – these MAbs inhibit end-processing, DNA joining and reintegration, and had little effect on disintegration. Nilsen *et al.* [1996]
- 7F11: There is another MAb with this name that binds to gp120. Lasky *et al.* [1987]

No. 230
MAb ID 8E5
HXB2 Location Integrase (262–271)
Author Location Integrase (262–271 HXB2)
Epitope RRKAKIIRDY
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade HXB2 *HIV component:* Int
Species (Isotype) mouse (IgG1κ)
References Nilsen *et al.* 1996; Haugan *et al.* 1995

- 8E5: A set of three MAbs recognize an epitope in this region, 7C3, 7F11, and 8E5 – all three HIV-1 MAbs cross-react with HIV-2 IN – these MAbs inhibit end-processing, DNA joining and reintegration, and had little effect on disintegration. Nilsen *et al.* [1996]
- 8E5: MAb interferes with integrase binding to DNA. Haugan *et al.* [1995]

No. 231
MAb ID MAb 35
HXB2 Location Integrase (264–273)
Author Location Integrase (264–273)
Epitope KAKIIRDYGK
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgGκ)
References Acel *et al.* 1998; Barsov *et al.* 1996

- MAb 35: Integrase was shown to have intrinsic DNA polymerase activity that can catalyze gap repair – MAb 35 inhibits this activity. Acel *et al.* [1998]
- MAb 35: There appears to be two different IN Abs with similar names: MAb 35 and 35. Barsov *et al.* [1996]
- MAb 35: Although MAb 35 does not inhibit HIV-1 IN, Fab 35 inhibits 3'-end processing, strand transfer and disintegration. Barsov *et al.* [1996]

IV-C-10 Pol Antibodies

No. 232
MAb ID 12
HXB2 Location Pol
Author Location Integrase (1–58)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG2a)
References Levy-Mintz *et al.* 1996; Bizub-Bender *et al.* 1994

- 12: Used for the creation of single-chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. Levy-Mintz *et al.* [1996]
- 12: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 12, 13 and 35 form a competition group. Bizub-Bender *et al.* [1994]

No. 233
MAb ID 13
HXB2 Location Pol
Author Location Integrase (1–58)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG1)
References Bizub-Bender *et al.* 1994

- 13: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 12, 13 and 35 form a competition group. Bizub-Bender *et al.* [1994]

No. 234
MAb ID 14
HXB2 Location Pol
Author Location Integrase (1–58)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG1)
References Bizub-Bender *et al.* 1994

- 14: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 14 and 17 form a competition group. Bizub-Bender *et al.* [1994]

No. 235
MAb ID 16
HXB2 Location Pol
Author Location Integrase
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG2a)
References Bizub-Bender *et al.* 1994

- 16: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized. Bizub-Bender *et al.* [1994]

No. 236
MAb ID 1C12B1
HXB2 Location Pol
Author Location RT (431–521)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* RT
Species (Isotype) mouse
References Ferns *et al.* 1991

- 1C12B1: UK Medical Research Council AIDS reagent: ARP384.
- 1C12B1: Recognized both p66 and p51 in Western blot, binds to C terminus. Ferns *et al.* [1991]

No. 237
MAb ID 21
HXB2 Location Pol
Author Location Integrase (58–141)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG2b)
References Levy-Mintz *et al.* 1996; Bizub-Bender *et al.* 1994

- 21: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. Levy-Mintz *et al.* [1996]
- 21: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized. Bizub-Bender *et al.* [1994]

No. 238
MAb ID 32 (mAb32, Fab32)
HXB2 Location Pol
Author Location Integrase (223–266)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG2b)
References Yi *et al.* 2002; Yi & Skalka 2000; Bizub-Bender *et al.* 1994

- 32: Called mAb32 – mAb33 and mAb32 compete for binding to the C-term domain of Integrase – while mAb32 only weakly inhibits IN activity, mAb33 inhibits strongly, mAb32 has a lower affinity than mAb33, and Fab32 does not inhibit at all while Fab33 inhibits DNA binding a catalytic activity. Yi *et al.* [2002]
- 32: Limited proteolysis combined with mass spectrometric analysis indicates Fab32 binds to two strands of the beta sheet, beta1 223F, 224R, 226Y, and 228R and beta5 264K and 266K. Yi & Skalka [2000]
- 32: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – MAbs 32 and 33 form a competition group. Bizub-Bender *et al.* [1994]

No. 239
MAb ID 35
HXB2 Location Pol
Author Location Integrase (1–58)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG2b)
References Bizub-Bender *et al.* 1994

- 35: There appears to be two IN Abs with similar names: MAb 35 and 35. Bizub-Bender *et al.* [1994]
- 35: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 12, 13 and 35 form a competition group. Bizub-Bender *et al.* [1994]

No. 240
MAb ID 3D12
HXB2 Location Pol
Author Location RT
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* RT
Species (Isotype) mouse (IgG2a)
References Chiba *et al.* 1997

- 3D12: There is an anti-Nef MAb that also has this name (see Chiba *et al.* [1997]) Chiba *et al.* [1997]

No. 241
MAb ID 3F10
HXB2 Location Pol
Author Location RT
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* RT
Species (Isotype) mouse (IgG2a)
References Chiba *et al.* 1997

No. 242
MAb ID 4
HXB2 Location Pol
Author Location Integrase (141–172)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG2b)
References Levy-Mintz *et al.* 1996; Bizub-Bender *et al.* 1994

- 4: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. Levy-Mintz *et al.* [1996]
- 4: There is another MAb with this ID that reacts with gp41. Bizub-Bender *et al.* [1994]
- 4: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – 4 has a low binding affinity. Bizub-Bender *et al.* [1994]

No. 243
MAb ID 6B9
HXB2 Location Pol
Author Location RT
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* RT
Species (Isotype) mouse (IgG2a)
References Chiba *et al.* 1997

No. 244
MAb ID 7C4
HXB2 Location Pol
Author Location RT
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* RT
Species (Isotype) mouse (IgG1)
References Chiba *et al.* 1997

- 7C4: Dose-dependent inhibition of polymerase activity of RT of strains IIIB, Bru and IMS-1, but not HIV-2 strains GH-1 or LAV-2 or SIV strains MAC or MND. Chiba *et al.* [1997]

No. 245
MAb ID RT-4
HXB2 Location Pol
Author Location RT
Epitope
Neutralizing no
Immunogen
Species (Isotype) mouse (IgG2b)
References Gu *et al.* 1996; Li *et al.* 1993

- RT-4: Increased nevirapine and delavirdine inhibition, no effect on AZT inhibition. Gu *et al.* [1996]

No. 246
MAb ID RT7O
HXB2 Location Pol

Author Location RT (231–315)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* RT
Species (Isotype) mouse (IgG1)
Research Contact B. Ferns and R. Tedder
References Ferns *et al.* 1991

- RT7O: UK Medical Research Council AIDS reagent: ARP381.
- RT7O: Conformational epitope located centrally in the protein – inhibited RT enzyme activity and thus may bind close to the active site of the enzyme. Ferns *et al.* [1991]

No. 247
MAb ID RT7U
HXB2 Location Pol
Author Location RT (231–315)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* RT
Species (Isotype) mouse
Research Contact B. Ferns and R. Tedder
References Ferns *et al.* 1991

- RT7U: UK Medical Research Council AIDS reagent: ARP380.
- RT7U: Has a conformational epitope – reacts with p66 and p51 in WB. Ferns *et al.* [1991]

No. 248
MAb ID anti-HIV-1 RT
HXB2 Location Pol
Author Location RT
Epitope
Neutralizing
Immunogen
Species (Isotype) mouse (IgG)
References Wainberg & Gu 1995; Maciejewski *et al.* 1995; di Marzo Veronese *et al.* 1986

- anti-HIV-1 RT: Cloned heavy and light chains to express Fab intracellularly, preventing HIV infection *in vitro* – this MAb was broadly cross-reactive with clinical strains and even HIV-2. Maciejewski *et al.* [1995]
- Commentary on Maciejewski *et al.* Wainberg & Gu [1995]

No. 249
MAb ID polyclonal
HXB2 Location Pol
Author Location p55
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* Gag, gp120, V3
Species (Isotype) macaque
References Wagner *et al.* 1998b

- A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains – gag and env CTL specific CTL were stimulated in each case, and Ab response to gag and gp120 and was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock. Wagner *et al.* [1998b]

No. 250
MAb ID polyclonal
HXB2 Location Pol
Author Location RT
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12
Species (Isotype) mouse
References Kim *et al.* 1997b

- A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice, as well as Ab response detected by ELISA. Kim *et al.* [1997b]

No. 251
MAb ID polyclonal
HXB2 Location Pol
Author Location RT (203–219)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: Salmonella *HIV component:* RT
Species (Isotype) mouse (IgA)
References Burnett *et al.* 2000

- A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV RT gene fragment in the Lpp-OmpA-HIV fusion protein, induced a lymphoproliferative Th response and fecal RT-specific IgA in BALB/c mice. Burnett *et al.* [2000]

No. 252
MAb ID 33 (mAb33, Fab33, 33D5, mab 33)
HXB2 Location Pol
Author Location Integrase (223–268 HXB2)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Int
Species (Isotype) mouse (IgG2b)
Ab Type C-term
References Yi *et al.* 2002; Yi & Skalka 2000; Levy-Mintz *et al.* 1996; Bizub-Bender *et al.* 1994

- 33: Called mAb33 – mAb33 and mAb32 compete for binding to the C-term domain of Integrase – while mAb32 only weakly inhibits IN activity, mAb33 inhibits strongly, mAb32 has a lower affinity than mAb33, and Fab32 does not inhibit at all while Fab33 inhibits catalytic activity and DNA binding – heteronuclear NMR indicated eight residues of Integrase are immobilized upon Fab33 binding, two in the core of the protein, and 6 on the outer face that form a contiguous patch likely to contain the epitope – 223F, 224R, 226Y, 244K, 267I, and 268I, which may be a useful target for drug design – the Fab33-IN complex is far more soluble than IN alone and may be useful for crystallization. Yi *et al.* [2002]
- 33: Limited proteolysis combined with mass spectrometric analysis were used to define the binding site for Fab32, but Fab33 binding to the Intergrase C-term domain left it resistant to proteolytic digestion. Yi & Skalka [2000]
- 33: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. Levy-Mintz *et al.* [1996]
- 33: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – MAbs 32 and 33 form a competition group. Bizub-Bender *et al.* [1994]

No. 253
MAb ID F-6
HXB2 Location Pol
Author Location RT (BH-10)
Epitope
Subtype B
Neutralizing
Immunogen in vitro stimulation or selection
Species (Isotype) human
Ab Type C-term
Research Contact Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal
References Herschhorn *et al.* 2003
Keywords antibody generation, antibody sequence, variable domain, immunotherapy

- F-6: One of five human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to bind to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. To pinpoint the mechanism of inhibition, three peptides were synthesized corresponding to the CDR3 sequences of F-6, and a cyclic version of the CDR H3 region bound to purified RT and blocked RDDP. Herschhorn *et al.* [2003] (**antibody generation**, **immunotherapy**, **antibody sequence, variable domain**)

IV-C-11 Vif Antibodies

No. 254
MAb ID TG002
HXB2 Location Vif (34–47)
Author Location Vif (34–47)
Epitope KARGWFYRHHYESP?
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Vif
Species (Isotype) mouse
Research Contact Transgene
References

- TG002: This MAb was raised in response to a rec Vif protein derived from E. coli.
- TG002: NIH AIDS Research and Reference Reagent Program: 2746.

No. 255
MAb ID TG001
HXB2 Location Vif (176–192)
Author Location Vif (176–192)
Epitope KPQKTKGHRGSHTMNGH?
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Vif
Species (Isotype) mouse
Ab Type C-term
Research Contact Transgene
References

- TG001: This antibody was raised in response to a rec Vif protein derived from E. coli.
- TG001: NIH AIDS Research and Reference Reagent Program: 2745.

No. 256
MAb ID J4
HXB2 Location Vif
Author Location (HXB2)
Epitope
Subtype B
Neutralizing
Immunogen
Species (Isotype) humanized rabbit
References Goncalves *et al.* 2002

- J4: The authors developed a Vif-specific intrabody single-chain FAb fragment of J4 called 14BL – when expressed intracellularly in the cytoplasm this intrabody efficiently bound Vif protein and neutralized its infectivity enhancing function – intrabody-expressing transduced cells were shown to be highly refractory to challenge with the laboratory strain NL43 and with primary isolates strains of HIV-1. Goncalves *et al.* [2002]

No. 257
MAb ID polyclonal
HXB2 Location Vif
Author Location Vif
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12
Species (Isotype) mouse
References Kim *et al.* 1997b

- A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice, as well as an Ab response detected by ELISA. Kim *et al.* [1997b]

IV-C-12 Vpr Antibodies

No. 258
MAb ID polyclonal
HXB2 Location Vpr
Author Location Vpr (89.6)
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Richardson *et al.* 2003
Country France
Keywords rate of progression

- Serum samples were obtained from the French GRIV (genetic resistance to HIV) cohort and tested for anti-Tat and anti-Vpr responses, as both may contribute as extracellular proteins to pathogenesis. Serum anti-Vpr IgG responses were significantly higher in stable non-progressors (CD4+ T cell counts greater than 500 cell/ul after being positive for 8 years with no ART) and unstable non-progressors (declined during a 20 month follow up), than fast progressors (CD4+ T less than 300 cells/ul within 2 years of seroconversion, some HAART). Serum anti-Tat IgG was found to be significantly higher in stable non-progressors compared to unstable non-progressors and fast progressors indicating that higher levels of serum anti-Tat IgG are associated with maintenance of non-progression status. Richardson *et al.* [2003] (**rate of progression**)

IV-C-13 Tat Antibodies

No. 259
MAb ID polyclonal
HXB2 Location Tat (1–15)
Author Location Tat (1–15 89.6)
Epitope MEPVDRPLEPWKHPG
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (Isotype) macaque (IgG)
Ab Type C-term, N-term, Tat basic region
References Silvera *et al.* 2002
Keywords antibody binding site definition and exposure, vaccine antigen design

- Anti-Tat and Tat toxoid responses were raised in rhesus macaques using HxBc2 and 89.6P Tat, and Tat toxoids.High anti-Tat IgG responses were observed in all animals, and helper responses were detected in 8/16, and IFN gamma CTL in 11/16.. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response. The most consistent reactions to the vaccinations were to peptides in regions: N-term, 1-15 (MEPVDRPLEPWKHPG), basic domain 46-60 (SYGRKKRRQRRRAHQ), and 61-91, particularly C-term 76-90 (QPRGDPTGPKQKKK). Silvera *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 260
MAb ID polyclonal
HXB2 Location Tat (1–20)
Author Location Tat (1–20 IIIB BH10)
Epitope MEPVDPRLEPWKHPGSQPKT?
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2)
Species (Isotype) mouse (IgA, IgG)
References Borsutzky *et al.* 2003
Keywords adjuvant comparison, genital and mucosal immunity, immunodominance, mucosal immunity, Th1, Th2, vaccine-induced epitopes

- Intranasal immunization of BALB/c mice Tat with MALP-2 induced stronger immune responses than i.p. vaccination of Tat with IFA. Also i.n. MALP-2 vaccination favored Th1 responses, while i.p IFA favored Th2. Ab, T help and CTL responses were observed. MALP-2 enhanced Tat-specific IgA responses in the lung and in the genital tract. Three linear Ab epitopes were recognized. The most frequent response (80% of vaginal lavage, 100% of sera and lung lavage) was to Tat peptide 1-20. The second strongest to Tat 46-60 (20% of vaginal lavage, 50% of lung lavage, 50% of sera). Finally, 50% of the sera of Tat+ IFA i.p. immunized mice recognized Tat 73-86. Borsutzky *et al.* [2003] (**adjuvant comparison**, **genital and mucosal immunity**, **vaccine-induced epitopes**, **immunodominance**, **mucosal immunity**, **Th1**, **Th2**)

No. 261
MAb ID TA9
HXB2 Location Tat (1–20)
Author Location Tat (1–20 Lai/Bru)
Epitope MEPVDPRLEPGSQPKT
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG)
Ab Type N-term

Research Contact Dr. J.-L. Guesdon, Institut Pasteur, Paris
References Belliard *et al.* 2003
Keywords inter-clade comparisons

- This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. TA9 is clade B specific, and does not recognize Tat from clade A, C, D, or CRF01 (AE).TA9 binds to the Tat peptide aa 1-61 strongly, and is also able to bind to Tat aa 1-20, and Tat peptide aa 8-53. Belliard *et al.* [2003] (**inter-clade comparisons**)

No. 262
MAb ID TD84
HXB2 Location Tat (1–20)
Author Location Tat (1–20 Lai/Bru)
Epitope MEPVDPRLEPGSQPKT
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG)
Ab Type N-term
Research Contact Dr. J.-L. Guesdon, Institut Pasteur, Paris
References Belliard *et al.* 2003
Keywords inter-clade comparisons

- This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. TD84 is clade B specific, and does not recognize Tat from clade A, C, D, or CRF01 (AE). It reacts strongly with aa 1-61, and is able to react with aa 1-20. Belliard *et al.* [2003] (**inter-clade comparisons**)

No. 263
MAb ID TE135
HXB2 Location Tat (1–20)
Author Location Tat (1–20 Lai/Bru)
Epitope MEPVDPRLEPGSQPKT
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG)
Ab Type N-term
Research Contact Dr. J.-L. Guesdon, Institut Pasteur, Paris
References Belliard *et al.* 2003
Keywords inter-clade comparisons

- This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. TE135 is clade B specific, and does not recognize Tat from clade A, C, D, or CRF01 (AE). It reacts strongly with aa 1-61, and is able to react with aa 1-20. Belliard *et al.* [2003] (**inter-clade comparisons**)

No. 264
MAb ID polyclonal
HXB2 Location Tat (1–24)
Author Location Tat (1–24)
Epitope MEPVDPRLEPWKHPGSQPKTACTN
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade *HIV component:* Tat *Adjuvant:* Montanide (ISA 51)
Species (Isotype) human (IgG)
Ab Type N-term
References Noonan *et al.* 2003
Keywords immunotherapy, vaccine-specific epitope characteristics

- Intramuscular injection of Tat-toxoid induced high titers of anti-Tat reactivity in serum samples of six HIV-1 positive and of four HIV negative study subjects. Anti-Tat antibodies successfully blocked extracellular Tat from transactivating HIV Tat-sensitive promotors. The anti-Tat IgG response in sera from two healthy and HIV infected patients inhibited cell entry of synthetic Tat, thus blocking its functional activity. Additionally, the anti-Tat antibodies inhibited intercellular Tat transfer as demonstrated by a co-culture cell system. All HIV-1 infected patients had Ab responses to the N-term region of Tat, and 4/4 HIV-1 + and 5/6 HIV-1 negative patients responded to the basic domain. Several additional peptides were recognized either exclusively or more commonly in the HIV+ people. The N-terminus region of Tat mediates binding to CD26, that may be involved in modulation of chemokine function, and may also mediate T-cell apotosis. Noonan *et al.* [2003] (**vaccine-specific epitope characteristics**, **immunotherapy**)

No. 265
MAb ID NT3/2D1.1
HXB2 Location Tat (2–15)
Author Location Tat
Epitope EPVDPNLEPWNHPS
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* Tat
Species (Isotype) mouse (IgG1a)
Ab Type N-term
References Dingwall *et al.* 1989

- NT3/2D1.1: UK Medical Research Council AIDS reagent: ARP352.
- NT3/2D1.1: Immunoprecipitates and immunoblots HIV-1 tat protein. Dingwall *et al.* [1989]

No. 266
MAb ID 1.2
HXB2 Location Tat (2–17)
Author Location Tat (1–16)
Epitope EPVDPRLEWKHPGSQ
Neutralizing
Immunogen
Species (Isotype)
References Ranki *et al.* 1995; Ovod *et al.* 1992

- 1.2: Weak expression of Tat observed in HIV+ brain tissue sample, in contrast to Nef. Ranki *et al.* [1995]

No. 267
MAb ID 1D9D5
HXB2 Location Tat (2–21)
Author Location Tat
Epitope EPVDPRLEWKHPGSQPKTA

Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Tat
Species (Isotype) mouse (IgG1)
Ab Type N-term
References Valvatne *et al.* 1996; Mhashilkar *et al.* 1995

- 1D9D5: Exogenously delivered Tat can efficiently transactivate an HIV-LTR-CAT construct in HeLa cells in the presence of 1D9D5, suggesting when considered with the results of Mhashilkar *et al.* [1995], that free Tat and not Ab bound is taken up by cells Valvatne *et al.* [1996]. Mhashilkar *et al.* [1995]; Valvatne *et al.* [1996]
- 1D9D5: Single chain antibodies, intrabodies, were engineered that can be stably expressed in the cytoplasm of mammalian cells – co-expression of an N-term intrabody can inhibit transactivation of an HIV LTR-CAT construct and block import into nucleus, but intrabody specific for exon 2 did not inhibit activity. Mhashilkar *et al.* [1995]

No. 268
MAb ID TB12
HXB2 Location Tat (44–60)
Author Location Tat (44–61 Lai/Bru)
Epitope GISYGRKKRRQRRPPQG
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG)
Ab Type Tat basic region
Research Contact Dr. J.-L. Guesdon, Institut Pasteur, Paris
References Belliard *et al.* 2003
Keywords inter-clade comparisons

- This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. TB12 is clade B and D specific, and does not recognize Tat from clade A, C, or CRF01 (AE). It reacts strongly with aa 1-61, and is also able to react with aa 44-61, in the basic region involved in Tat uptake. Belliard *et al.* [2003] (**inter-clade comparisons**)

No. 269
MAb ID polyclonal
HXB2 Location Tat (46–60)
Author Location Tat (46–60 IIIB BH10)
Epitope SYGRKKRRQRRRAHQ?
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2)
Species (Isotype) mouse (IgA, IgG)
References Borsutzky *et al.* 2003
Keywords adjuvant comparison, genital and mucosal immunity, immunodominance, mucosal immunity, Th1, Th2, vaccine-induced epitopes

- Intranasal immunization of BALB/c mice Tat with MALP-2 induced stronger immune responses than i.p. vaccination of Tat with IFA. Also i.n. MALP-2 vaccination favored Th1 responses, while i.p IFA favored Th2. Ab, T help and CTL responses were observed. MALP-2 enhanced Tat-specific IgA responses in the lung and in the genital tract. Three linear Ab epitopes were recognized. The most frequent response (80% of vaginal lavage, 100% of sera and lung lavage) was to Tat peptide 1-20. The second strongest to Tat 46-60 (20% of vaginal lavage, 50% of lung lavage, 50% of sera). Finally, 50% of the sera of Tat+ IFA i.p. immunized mice recognized Tat 73-86. Borsutzky *et al.* [2003] (**adjuvant comparison**, **genital and mucosal immunity**, **vaccine-induced epitopes**, **immunodominance**, **mucosal immunity**, **Th1**, **Th2**)

No. 270
MAb ID polyclonal
HXB2 Location Tat (46–60)
Author Location Tat (46–60 89.6)
Epitope SYGRKKRRQRRRAHQ
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (Isotype) macaque (IgG)
Ab Type C-term, N-term, Tat basic region
References Silvera *et al.* 2002
Keywords antibody binding site definition and exposure, vaccine antigen design

- Anti-Tat and Tat toxoid responses were raised in rhesus macaques using HxBc2 and 89.6P Tat, and Tat toxoids.High anti-Tat IgG responses were observed in all animals, and helper responses were detected in 8/16, and IFN gamma CTL in 11/16.. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response. The most consistent reactions to the vaccinations were to peptides in regions: N-term, 1-15 (MEPVDRPLEPWKHPG), basic domain 46-60 (SYGRKKRRQRRRAHQ), and 61-91, particularly C-term 76-90 (QPRGDPTGPKQKKK). Silvera *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 271
MAb ID polyclonal
HXB2 Location Tat (46–60)
Author Location Tat (46–60 89.6)
Epitope SYGRKKRRQRRRAHQ
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (Isotype) macaque (IgG)
Ab Type C-term, N-term, Tat basic region
References Silvera *et al.* 2002

Keywords antibody binding site definition and exposure, vaccine antigen design

- Anti-Tat and Tat toxoid responses were raised in rhesus macaques using HxBc2 and 89.6P Tat, and Tat toxoids.High anti-Tat IgG responses were observed in all animals, and helper responses were detected in 8/16, and IFN gamma CTL in 11/16.. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response. The most consistent reactions to the vaccinations were to peptides in regions: N-term, 1-15 (MEPVDRPLEPWKHPG), basic domain 46-60 (SYGRKKRRQRRRAHQ), and 61-91, particularly C-term 76-90 (QPRGDPTGPKQKKK). Silvera *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 272
MAb ID polyclonal
HXB2 Location Tat (47–60)
Author Location Tat (46–60)
Epitope YGRKKRRQRRRPPQ
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade *HIV component:* Tat *Adjuvant:* Montanide (ISA 51)
Species (Isotype) human (IgG)
Ab Type Tat basic region
References Noonan *et al.* 2003
Keywords immunotherapy, vaccine-specific epitope characteristics

- Intramuscular injection of Tat-toxoid induced high titers of anti-Tat reactivity in serum samples of six HIV-1 positive and of four HIV negative study subjects. Anti-Tat Abs successfully blocked extracellular Tat from transactivating HIV Tat-sensitive promotors. The anti-Tat IgG response in sera from two healthy and HIV infected patients inhibited cell entry of synthetic Tat, thus blocking its functional activity. Additionally, the anti-Tat Abs inhibited intercellular Tat transfer in a co-culture cell system. All HIV-1 infected patients had Ab responses to the N-term region of Tat, and 4/4 HIV-1 + and 5/6 HIV-1 negative patients responded to the basic domain. Several additional peptides were recognized either exclusively or more commonly in the HIV+ people. The basic region of Tat mediates binding to VEGFR2 on Kaposi's sarcoma cells and endothelial cells, and HIV patients with Kaposi's sarcoma lack Abs to this domain. Noonan *et al.* [2003] (**vaccine-specific epitope characteristics**, **immunotherapy**)

No. 273
MAb ID 1D2F11
HXB2 Location Tat (49–86)
Author Location Tat
Epitope RKKRRQRRRPPQGSQTHQVSLSKQPTSQSRGDPTGPKE
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Tat
Species (Isotype) mouse (IgG1)
Ab Type C-term
References Valvatne *et al.* 1996

- 1D2F11: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat. Valvatne *et al.* [1996]

No. 274
MAb ID 2D9E7
HXB2 Location Tat (49–86)
Author Location Tat
Epitope RKKRRQRRRPPQGSQTHQVSLSKQPTSQSRGDPTGPKE
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Tat
Species (Isotype) mouse (IgG1)
Ab Type C-term
References Valvatne *et al.* 1996

- 2D9E7: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat, but less efficiently than MAbs 1D2F11 or 4B4C4. Valvatne *et al.* [1996]

No. 275
MAb ID 4B4C4 (4B4)
HXB2 Location Tat (49–86)
Author Location Tat
Epitope RKKRRQRRRPPQGSQTHQVSLSKQPTSQSRGDPTGPKE
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Tat
Species (Isotype) mouse (IgG1)
Ab Type C-term
References Jensen *et al.* 1997; Valvatne *et al.* 1996

- 4B4C4: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat. Valvatne *et al.* [1996]

No. 276
MAb ID 5G7D8
HXB2 Location Tat (49–86)
Author Location Tat
Epitope RKKRRQRRRPPQGSQTHQVSLSKQPTSQSRGDPTGPKE
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Tat
Species (Isotype) mouse (IgG1)
Ab Type C-term
References Valvatne *et al.* 1996

- 5G7D8: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat, but less efficiently than 1D2F11 or 4B4C4. Valvatne *et al.* [1996]

No. 277
MAb ID polyclonal
HXB2 Location Tat (73–86)
Author Location Tat (73–86 IIIB BH10)
Epitope PTSQPRGDPTGPKE?
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2)
Species (Isotype) mouse (IgA, IgG)
References Borsutzky *et al.* 2003
Keywords adjuvant comparison, genital and mucosal immunity, immunodominance, mucosal immunity, Th1, Th2, vaccine-induced epitopes

- Intranasal immunization of BALB/c mice Tat with MALP-2 induced stronger immune responses than i.p. vaccination of Tat with IFA. Also i.n. MALP-2 vaccination favored Th1 responses, while i.p IFA favored Th2. Ab, T help and CTL responses were observed. MALP-2 enhanced Tat-specific IgA responses in the lung and in the genital tract. Three linear Ab epitopes were recognized. The most frequent response (80% of vaginal lavage, 100% of sera and lung lavage) was to Tat peptide 1-20. The second strongest to Tat 46-60 (20% of vaginal lavage, 50% of lung lavage, 50% of sera). Finally, 50% of the sera of Tat+ IFA i.p. immunized mice recognized Tat 73-86. Borsutzky *et al.* [2003] (**adjuvant comparison**, **genital and mucosal immunity**, **vaccine-induced epitopes**, **immunodominance**, **mucosal immunity**, **Th1**, **Th2**)

No. 278
MAb ID NT2/4D5.24
HXB2 Location Tat (73–86)
Author Location Tat
Epitope PTSQPRGDPTGPKE
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* Tat
Species (Isotype) mouse
Ab Type C-term
References Dingwall *et al.* 1989

- NT2/4D5.24: Immunoprecipitates and immunoblots HIV-1 tat protein. Dingwall *et al.* [1989]

No. 279
MAb ID polyclonal
HXB2 Location Tat (76–89)
Author Location Tat (76–90 89.6)
Epitope QPRGDPTGPKQKKK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Species (Isotype) macaque (IgG)
Ab Type C-term, N-term, Tat basic region
References Silvera *et al.* 2002
Keywords antibody binding site definition and exposure, vaccine antigen design

- Anti-Tat and Tat toxoid responses were raised in rhesus macaques using HxBc2 and 89.6P Tat, and Tat toxoids.High anti-Tat IgG responses were observed in all animals, and helper responses were detected in 8/16, and IFN gamma CTL in 11/16.. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response. The most consistent reactions to the vaccinations were to peptides in regions: N-term, 1-15 (MEPVDRPLEPWKHPG), basic domain 46-60 (SYGRKKRRQRRRAHQ), and 61-91, particularly C-term 76-90 (QPRGDPTGPKQKKK). Silvera *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 280
MAb ID
HXB2 Location Tat
Author Location Tat
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 51)
Species (Isotype) human
References Gringeri *et al.* 1998
Keywords immunotherapy

- 14 HIV-1 infected individuals were vaccinated with inactivated Tat (called Tat-toxoid), with the intent of enhancing Tat Ab levels to suppress the negative impact of secreted Tat on immune function. Tat vaccinations were safe and patients developed increased levels of Tat-specific Abs; some patients had increased Tat-specific proliferative responses. CD4 T cells tended to increase a small but significant amount after immunization, and in several patients viral load decreased. Gringeri *et al.* [1998] (**immunotherapy**)

No. 281
MAb ID L-anti-Tat
HXB2 Location Tat
Author Location Tat
Epitope
Neutralizing L P (when lipidated)
Immunogen Vaccine
Vector/Type: protein *HIV component:* Tat
Species (Isotype) mouse (IgG1)
Research Contact AGMED, Inc., Bedford, MA USA
References Cruikshank *et al.* 1997

- L-anti-Tat: Lipidated antibody can be taken up by cells and effectively block IIIB and primary virus HIV-1 replication in actively and latently infected cells. Cruikshank *et al.* [1997]

No. 282
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat

Epitope
Subtype A, B, C, CRF01_AE, D
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Belliard *et al.* 2003
Country France
Keywords inter-clade comparisons, rate of progression

- Sera from 20 HIV-1 positive individuals were tested for their ability to react with Tat proteins from different clades, and were found to react with subtype A, B, and D, but not with subtype C or CRF01 (AE). Sera from 101 slow progressors and 42 fast progressors were tested for responses to Tat peptides, and compared to responses to gp41 peptide, as anti-Tat antibodies have been shown by others to be elevated in slow progressors. In this study, overall levels of Tat antibodies were not different in the two groups, however relative levels of antibodies to different Tat and gp41 peptides were observed. Belliard *et al.* [2003] (**inter-clade comparisons**, **rate of progression**)

No. 283
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA), red blood cells
Species (Isotype) mouse (IgG1, IgG2a, IgG3)
References Dominici *et al.* 2003
Keywords adjuvant comparison, immunotherapy, Th1, Th2

- BALB/c mice were immunized intra-peritineally with Tat protein bound to red blood cells via biotin-avidin conjugation. This antigen delivery system was successfully internalized by dendritic cells, and induced more consistent anti-Tat NAbs responses and sightly increased Tat-specific CTL responses relative to Tat protein with CFA. RBC-Tat immunization induced Th1 (IgG2a)and Th2 (IgG1 and IgG3)type immune responses. (**adjuvant comparison**, **immunotherapy**, **Th1**, **Th2**)

No. 284
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chitosan nanoparticles *HIV component:* Tat *Adjuvant:* adjuvant oily structure (IMS)
Species (Isotype) mouse (IgA, IgG)
References Le Buanec *et al.* 2001
Keywords adjuvant comparison, mucosal immunity

- Mice were immunized with Tat toxoid (Tat detoxified by carboxamidation) either intranasally or orally using either adjuvant oily structure (IMS), nanoparticles of chitosan, or microparticles of polylactide-co-glycolide. Each of these strategies triggered IgG and IgA that inhibited Tat activity. Le Buanec *et al.* [2001] (**adjuvant comparison**, **mucosal immunity**)

No. 285
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat (IIIB)
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Cholera toxin (CT), E. coli mutant heat labile enterotoxin (LT-R72), E. coli heat labile enterotoxin
Species (Isotype) mouse (IgG)
References Marinaro *et al.* 2003
Keywords adjuvant comparison, mucosal immunity

- Intranasal immunization of BALB/c mice with Tat and e.coli heat-labile enterotoxin (LT) and non-toxic LT-R72 LT induced strong antigen-specific IgG Abs which remained stable for one year. Tat-specific IgA reponses were measured in vaginal and intestinal secretions. Immunization of BALB/c mice with native Tat (aa1-86) induced serum IgG directed against an immunodominant epitope (aa1-20) and against a second epitope (aa 46-60). CTL responses were also observed. Anti-Tat serum Abs neutralized Tat activity in a dose-independent manner. C57BL/6 remained unresponsive to Tat immunizations when Tat was co-adminstered with LT or cholera toxin (CT) as adjuvant; BALB/c mice are H-2d, C57BL/6 are H-2b. Congenic BALB.C mice that express H-2b rather than H-2d also could not respond to Tat, suggesting the repsonse to Tat is constrained by the haplotype. Marinaro *et al.* [2003] (**adjuvant comparison**, **mucosal immunity**)

No. 286
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein, vaccinia *Strain:* B clade MN *HIV component:* gp160, Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), polyphosphazene
Species (Isotype) macaque (IgG)
References Pauza *et al.* 2000

- 16 Macaques mulatta were immunized with Tat toxoid, or with Tat plus gp160, and challenged with the SHIV 89.6PD isolate. Sera from 14/16 animals neutralized Tat *in vitro*. 8 macaques developed both cellular and humoral responses to Tat, and 7/8 of these had low viral set points after rectal challenge with SHIV89.6PD. CD4+ T cells in Tat vaccinated infected animals

had lower IFN-alpha and chemokine receptor expression, features of infection associated with extracellular Tat. Pauza *et al.* [2000]

No. 287
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10 *HIV component:* gp120, Nef, Tat *Adjuvant:* AS02A (oil-in-water emulsion, 3D-monophosphoryl lipid A, QS21), AS06 (CpG, aluminum hydroxide)
Species (Isotype) macaque (IgG)
References Voss *et al.* 2003
Keywords adjuvant comparison, variant cross-recognition or cross-neutralization

- Monkeys were immunized with different combinations of gp120/NefTat/SIV-Tat three times over a three-month time period and intravenously challenged with SHIV 89.6P four weeks after the last immunzation. Vaccination induced anti-Tat, -Nef and -gp120 Ab responses that decreased until challenge. Neutralizing Ab responses against HIV-1 MN and HIV-1 W61D were observed. Vaccination with the combination of all three proteins reduced viral load and kept animals from a CD4+ T cell decline, preventing AIDS for more than 2.5 years. The adjuvant AS02A elicited NAbs and protected from disease, while AS06 did not. gp120 alone or TatNef/SIV-Tat without gp120 could not protect from disease. Voss *et al.* [2003] (**adjuvant comparison**, **variant cross-recognition or cross-neutralization**)

No. 288
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Zagury *et al.* 1998
Country France
Keywords immunotherapy, rate of progression

- Comparing 67 fast progressors with 182 non-progressors in the GRIV cohort, only anti-Tat Ab levels, not Abs to Env, Gag, or Nef, were correlated as a serological indicator of rate of progression. This suggests that raising Tat Abs may be beneficial as immunotherapy or in a vaccine. Zagury *et al.* [1998] (**immunotherapy**, **rate of progression**)

No. 289
MAb ID 2D9D5
HXB2 Location Tat
Author Location Tat
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Tat
Species (Isotype) mouse (IgG)
Ab Type C-term
References Mhashilkar *et al.* 1995

- 2D9D5: Single chain antibodies, intrabodies, were engineered that can be stably expressed in the cytoplasm of mammalian cells – co-expression of C-term intrabody did not inhibit transactivation of an HIV LTR-CAT construct, in contrast to MAb 1D9D5. Mhashilkar *et al.* [1995]

No. 290
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat (IIIB, 89.6, CMU08)
Epitope
Subtype B, CRF01_AE
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade *HIV component:* Tat
Species (Isotype) human (IgG)
Ab Type C-term, N-term, Tat basic region
References Richardson *et al.* 2003
Country France
Keywords antibody binding site definition and exposure, inter-clade comparisons, rate of progression, vaccine-specific epitope characteristics

- Serum samples were obtained from the French GRIV (genetic resistance to HIV) cohort and tested for anti-Tat and anti-Vpr responses as both may contribute as extracellular proteins to pathogenesis. Serum anti-Tat IgG responses were significantly higher and maintained for up to 20 months in stable non-progressors (CD4+ T cell counts greater than 500 cell/ul after being positive for 8 years with no ART) compared to unstable non-progressors and fast progressors (CD4+ T less than 300 cells/ul within 2 years of seroconversion, some HAART). Anti-Tat IgG from GRIV stable non-progressors recognized linear epitopes located within the N-terminal, basic and the C-terminal domains of Tat. Humoral responses of fast-progressors and of one unstable non-progressor were restricted to the basic region of Tat. Tat toxoid vaccinees from Milan tended to recognize N-terminal and C-terminal domains. Sera from some GRIV and Tat toxoid vaccinees cross-reacted in an ELISA assay with a truncated 89.6 S/HIV 89.6P Tat, 89.6P Tat, HIv-1 subtype E (CMU08) and with SIVmac251 Tat (one sample). Richardson *et al.* [2003] (**antibody binding site definition and exposure**, **vaccine-specific epitope characteristics**, **inter-clade comparisons**, **rate of progression**)

No. 291
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat
Epitope
Subtype B, CRF01_AE
Neutralizing
Immunogen Vaccine

Vector/Type: protein *Strain:* B clade 89.6, B clade IIIB *HIV component:* Tat
Species (Isotype) macaque (IgG)
Ab Type C-term, N-term, Tat basic region
References Richardson *et al.* 2002
Keywords antibody binding site definition and exposure, vaccine antigen design, variant cross-recognition or cross-neutralization

- Anti-Tat responses were raised in rhesus macaques using IIIB Tat, SHIV89.6P Tat, carboxymethylated Tat and 89.6P Tat toxoids. Tat IgG responses to the vaccine were cross-reactive with subtype E and MAC 251. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response and were not distinguishable from controls. Richardson *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**, **variant cross-recognition or cross-neutralization**)

No. 292
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat (IIIB, 89.6, CMU08)
Epitope
Subtype B, CRF01_AE
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade *HIV component:* Tat
Species (Isotype) human (IgG)
Ab Type C-term, N-term, Tat basic region
References Richardson *et al.* 2003
Country France
Keywords antibody binding site definition and exposure, inter-clade comparisons, rate of progression, vaccine-specific epitope characteristics

- Serum samples were obtained from the French GRIV (genetic resistance to HIV) cohort and tested for anti-Tat and anti-Vpr responses as both may contribute as extracellular proteins to pathogenesis. Serum anti-Tat IgG responses were significantly higher and maintained for up to 20 months in stable non-progressors (CD4+ T cell counts greater than 500 cell/ul after being positive for 8 years with no ART) compared to unstable non-progressors and fast progressors (CD4+ T less than 300 cells/ul within 2 years of seroconversion, some HAART). Anti-Tat IgG from GRIV stable non-progressors recognized linear epitopes located within the N-terminal, basic and the C-terminal domains of Tat. Humoral responses of fast-progressors and of one unstable non-progressor were restricted to the basic region of Tat. Tat toxoid vaccinees from Milan tended to recognize N-terminal and C-terminal domains. Sera from some GRIV and Tat toxoid vaccinees cross-reacted in an ELISA assay with a truncated 89.6 S/HIV 89.6P Tat, 89.6P Tat, HIv-1 subtype E (CMU08) and with SIVmac251 Tat (one sample). Richardson *et al.* [2003] (**antibody binding site definition and exposure**, **vaccine-specific epitope characteristics**, **inter-clade comparisons**, **rate of progression**)

No. 293
MAb ID G1
HXB2 Location Tat
Author Location Tat (1–15)
Epitope
Subtype B
Neutralizing yes
Immunogen Vaccine
Strain: B clade *HIV component:* Tat
Species (Isotype) human (IgG1κ)
Ab Type N-term
References Moreau *et al.* 2004
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, inter-clade comparisons

- G1: G1 is a single-chain fragment-variable scFv antibody derived from a Tat-toxoid vaccinated uninfected volunteer. G1 binds strongly to soluble rTAT protein and to denatured rTAT, suggesting that the epitope is linear. G1 recognized HIV-1 clade B Tat proteins Bru and HXB2, but did not bind to clade E (CM240), clade C (92Br), clade D (Eli) and clade A (Ug11RP). G1 inhibited Tat-transactivation of viral replication. The VH3 heavy chains of the two phage scFvG1 VH3 heavy chain sequences of scFvG1 and scFvG2 vary (G1 CDR3, RGSTGKALDYCSPRTL; G2 CDR3, ERSQQHCNPLLHSNGKNYAE) although both share identical Vk light chain sequences. Moreau *et al.* [2004] (**antibody binding site definition and exposure**, **inter-clade comparisons**, **antibody sequence, variable domain**)

No. 294
MAb ID G2
HXB2 Location Tat
Author Location Tat (1–15)
Epitope
Subtype B
Neutralizing yes
Immunogen Vaccine
Strain: B clade *HIV component:* Tat
Species (Isotype) human (IgG1κ)
Ab Type N-term
References Moreau *et al.* 2004
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, inter-clade comparisons

- G2: G2 is a single-chain fragment-variable scFv antibody derived from a Tat-toxoid vaccinated uninfected volunteer. G2 binds strongly to soluble rTAT protein and to denatured rTAT, suggesting that the epitope is linear. G2 recognized HIV-1 clade B Tat proteins Bru and HXB2, but did not bind to clade E (CM240), clade C (92Br), clade D (Eli) and clade A (Ug11RP). G2 inhibited Tat-transactivation of viral replication. The VH3 heavy chains of the two phage scFvG1 VH3 heavy chain sequences of scFvG1 and scFvG2 vary (G1 CDR3, RGSTGKALDYCSPRTL; G2 CDR3, ERSQQHCNPLLHSNGKNYAE) although both share identical Vk light chain sequences and Tat binding sites. Moreau *et al.* [2004] (**antibody binding site definition and exposure**, **inter-clade comparisons**, **antibody sequence, variable domain**)

No. 295

MAb ID J1
HXB2 Location Tat
Author Location Tat (1–15)
Epitope
Subtype B
Neutralizing yes
Immunogen Vaccine
Strain: B clade *HIV component:* Tat
Species (Isotype) human (IgG1λ)
Ab Type N-term
References Moreau *et al.* 2004
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, inter-clade comparisons

- J1: J1 is a single-chain fragment-variable scFv antibody derived from a Tat-toxoid vaccinated uninfected volunteer. J1 binds strongly to soluble rTAT protein and to denatured rTAT, suggesting that the epitope is linear. J1 recognized HIV-1 clade B Tat proteins Bru and HXB2, but did not bind to clade E (CM240), clade C (92Br), clade D (Eli) and clade A (Ug11RP). J1 inhibited Tat-transactivation of viral replication. Of three scFv antibodies, all bound the N-terminal amino acids 1-15, but G1 and G2 had kappa light chains and J1 had lambda, and the CDR3 of each was distinct, with J1's CDR3 sequence being: RDRYCSSPGCYKGADGGRLKDY. Moreau *et al.* [2004] (**antibody binding site definition and exposure**, **inter-clade comparisons**, **antibody sequence, variable domain**)

No. 296
MAb ID TC15
HXB2 Location Tat
Author Location Tat (Lai/Bru)
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG)
Ab Type N-term
Research Contact Dr. J.-L. Guesdon, Institut Pasteur, Paris
References Belliard *et al.* 2003
Keywords inter-clade comparisons

- TC15: This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. It is conformational reacting only with intact protein. It reacts with B and D clade Tat proteins, and does not recognize Tat from clade A, C, or CRF01 (AE). Belliard *et al.* [2003] (**inter-clade comparisons**)

No. 297
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat (Lai/Bru)
Epitope
Subtype B
Neutralizing
Immunogen SHIV infection, Vaccine
Vector/Type: peptide *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* aluminum phosphate, CpG immunostimulatory sequence (ISS), Montanide (ISA 720)
Species (Isotype) macaque (IgG)
Ab Type N-term
References Belliard *et al.* 2003
Keywords rate of progression

- Macaques were immunized with different combinations of Tat peptides. Serum from these animals was able to inhibit Tat-induced apoptosis, and Tat antibodies are associated with long term survival. Anti-Tat antibodies generated in infected macaques tended to be restricted to the peptide 44-61, while sera from infected humans could react with several different peptides. Belliard *et al.* [2003] (**rate of progression**)

No. 298
MAb ID polyclonal
HXB2 Location Tat
Author Location Tat (Lai/Bru)
Epitope
Subtype B
Neutralizing
Immunogen SHIV infection, Vaccine
Vector/Type: peptide *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* BSA, Complete Freund's Adjuvant (CFA)
Species (Isotype) rabbit (IgG)
Ab Type N-term
References Belliard *et al.* 2003
Keywords rate of progression

- 12 rabbits were immunized with different combinations of Tat peptides. Abs raised against peptide aa 8-53 did not react with the peptide 19-53, suggesting that the N-terminal region is important. Serum from these animals was able to inhibit Tat-induced apoptosis, and Tat antibodies in humans are associated with long term survival. Belliard *et al.* [2003] (**rate of progression**)

No. 299
MAb ID B1E3
HXB2 Location Tat
Author Location Tat (44–61)
Epitope
Subtype B
Neutralizing yes
Immunogen Vaccine
Strain: B clade *HIV component:* Tat
Species (Isotype) human (IgG1κ)
Ab Type Tat basic region
References Moreau *et al.* 2004
Keywords antibody binding site definition and exposure, inter-clade comparisons

- B1E3: B1E3 is a MAb derived from a Tat-toxoid vaccinated uninfected volunteer. B1E3 recognized two Tat peptides, aa19-53 and aa44-61 of an unspecified HIV-1 clade B Tat protein. B1E3 demonstrates a weak binding affinity to rTAT protein in solution, suggesting that epitope recognition may be conformation dependent B1E3 did not recognize synthetic HIV-1 clade B Tat proteins Bru and HXB2, clade E (CM240), clade

C (92Br), clade D (Eli) and clade A (Ug11RP). It only bound to native TAT protein, and could inhibit Tat-transactivation. Moreau *et al.* [2004] (**antibody binding site definition and exposure**, **inter-clade comparisons**)

No. 300
MAb ID J3B2
HXB2 Location Tat
Author Location Tat (44–61)
Epitope
Subtype B
Neutralizing yes
Immunogen Vaccine
Strain: B clade *HIV component:* Tat
Species (Isotype) human (IgG1λ)
Ab Type Tat basic region
References Moreau *et al.* 2004
Keywords antibody binding site definition and exposure, inter-clade comparisons

- J3B2: J3B2 is a MAb derived from a Tat-toxoid vaccinated uninfected volunteer. B1E3 recognized two Tat peptides, aa33-37 and aa37-51 of an unspecified HIV-1 clade B Tat protein. J3B2 demonstrates a weak binding affinity to rTAT protein in solution, suggesting that epitope recognition may be conformation dependent, B1E3 did not recognize synthetic HIV-1 clade B Tat proteins Bru and HXB2, clade E (CM240), clade C (92Br), clade D (Eli) and clade A (Ug11RP). It only bound to native TAT protein, and could inhibit Tat-transactivation. Moreau *et al.* [2004] (**antibody binding site definition and exposure**, **inter-clade comparisons**)

IV-C-14 Rev Antibodies

No. 301
MAb ID 4G9
HXB2 Location Rev (5–15)
Author Location Rev (5–15)
Epitope SGDSDEELIRT?
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) mouse
References Jensen *et al.* 1997

- 4G9: Mapped binding location by protein footprinting. Jensen *et al.* [1997]

No. 302
MAb ID Ab2
HXB2 Location Rev (32–50)
Author Location Rev (32–49 BRU)
Epitope EGTRQARRNRRRWRERQR
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) (IgG1)
Research Contact Tony Lowe and Jonathan Karn, MRC Center, Cambridge
References Henderson & Percipalle 1997

- Ab2: The Ab2 binding site overlaps the nuclear localization signal – Ab2 binding to Rev was blocked by bound HIV RNA – the cellular protein importin-beta can bind in this Arg rich region – atypically, the Rev binds specifically to importin-beta, but not to the importin-beta-importin-alpha dimer. Henderson & Percipalle [1997]

No. 303
MAb ID 10.1
HXB2 Location Rev (33–48)
Author Location Rev (33–48)
Epitope GTRQARRNRRRRWRER?
Neutralizing
Immunogen
Species (Isotype)
References Maksiutov *et al.* 2002; Ranki *et al.* 1995; Ranki *et al.* 1994; Ovod *et al.* 1992

- 10.1: This epitope is similar to a fragment of the human protein Complement 4 (containing C4A anaphlylatoxin), GRRNRRRR. Maksiutov *et al.* [2002]
- 10.1: Binds to the RRE binding site – polyclonal anti-Rev Ab detected Rev in astrocytes in 4/5 brain autopsy samples, but only one of these was positive using 10.1, suggesting most Rev was bound to RRE. Ranki *et al.* [1995]

No. 304
MAb ID 3H6
HXB2 Location Rev (38–43)
Author Location Rev (38–44)
Epitope RRNRRR
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) mouse (IgG1κ)
References Maksiutov *et al.* 2002; Orsini *et al.* 1995

- 3H6: There is another MAb with this ID that recognizes gp41.
- 3H6: This epitope is similar to a fragment of the human protein Complement 4 (containing C4A anaphlylatoxin), GRRNRRRR. Maksiutov *et al.* [2002]
- 3H6: Directed against nucleolar localization/RRE binding domain – antigenic domain tentative, MAb failed to bind a RRNRRR Rev deletion mutant. Orsini *et al.* [1995]

No. 305
MAb ID 8E7
HXB2 Location Rev (70–84)
Author Location Rev (70–84)
Epitope PVPLQLPPLERLTLD
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) mouse (IgG2aκ)
References Maksiutov *et al.* 2002; Boe *et al.* 1998; Jensen *et al.* 1997; Szilvay *et al.* 1995; Kalland *et al.* 1994b; Kalland *et al.* 1994a

- 8E7: This epitope is similar fragments of the human protein Epidermal growth factor receptor substrate 15, EPVPMSLPPA, and Insulin-like growth factor binding protein complex acid labile chain precursor, QPPGLERLWLEGNPWDCG. Maksiutov *et al.* [2002]

- 8E7: HIV-1 RNA and Rev localize to the same region in the nucleoplasm, but the splicing factor SC-35 localizes in different speckles with the nucleoplasm than Rev – intron containing beta-globin was distributed similarly to HIV-1, suggesting Rev and HIV-1 RNAs interact at putative sites of mRNA transcriptions and splicing. Boe *et al.* [1998]
- 8E7: Peptide interaction mapped to aa 70-84, 75-88 – protein footprint to 65-88. Jensen *et al.* [1997]
- 8E7: 8E7 worked in indirect immunofluorescence and also detected Rev in WB assays – used to detect localization of Rev in several compartments including the nucleoli, nucleoplasm, perinuclear zone, and cytoplasm – Rev co-localized with host cell factors known to assemble on nascent transcripts – Rev shuttles continuously between cytoplasmic and nucleoplasmic compartments. Kalland *et al.* [1994a,b]; Szilvay *et al.* [1995]

No. 306
MAb ID 9G2 (9G2G4D6E8)
HXB2 Location Rev (70–84)
Author Location Rev (70–84)
Epitope PVPLQLPPLERLTLD
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) mouse (IgG2aκ)
Research Contact Anne Marie Szilvay
References Maksiutov *et al.* 2002; Jensen *et al.* 1997; Kalland *et al.* 1994a

- 9G2: Called 9G2G4D6E8: UK Medical Research Council AIDS reagent: ARP3058.
- 9G2: This epitope is similar fragments of the human protein Epidermal growth factor receptor substrate 15, EPVPMSLPPA, and Insulin-like growth factor binding protein complex acid labile chain precursor, QPPGLERLWLEGNPWDCG. Maksiutov *et al.* [2002]
- 9G2: Peptide interaction mapped to aa 70-84, 75-88 – protein footprint to 65-88. Jensen *et al.* [1997]
- 9G2: Worked in indirect immunofluorescence and also detected Rev in WB assays – used to detect localization of Rev throughout the cell. Kalland *et al.* [1994a]

No. 307
MAb ID Ab4
HXB2 Location Rev (72–91)
Author Location Rev (72–91 BRU)
Epitope PLQLPPLERLTLDCNEDCGT
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) (IgG1)
Research Contact Tony Lowe and Jonathan Karn, MRC Center, Cambridge
References Maksiutov *et al.* 2002; Henderson & Percipalle 1997

- Ab4: This epitope is similar fragments of the human protein Epidermal growth factor receptor substrate 15, EPVPMSLPPA, and Insulin-like growth factor binding protein complex acid labile chain precursor, QPPGLERLWLEGNPWDCG. Maksiutov *et al.* [2002]
- Ab4: The binding site overlaps the nuclear export signal – binding was not blocked by bound HIV RNA and may be accessible for protein interaction. Henderson & Percipalle [1997]

No. 308
MAb ID 3G4
HXB2 Location Rev (90–116)
Author Location Rev (90–116)
Epitope GTSGTQGVGSPQILVESPTVLESGTKE?
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) mouse (IgG1κ)
References Orsini *et al.* 1995

- 3G4: Binds to a region that can be dispensed with and still retain Rev function. Orsini *et al.* [1995]

No. 309
MAb ID 1G10 (IG10F4)
HXB2 Location Rev (96–105)
Author Location Rev (95–105)
Epitope GVGSPQILVE
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) mouse (IgG2bκ)
Research Contact Anne Marie Szilvay
References Jensen *et al.* 1997; Kalland *et al.* 1994a

- 1G10: Called IG10F4: UK Medical Research Council AIDS reagent: ARP3060.
- 1G10: Peptide interaction mapped to aa 91-105, 96-110 – protein footprint to aa 10-20, and 95-105. Jensen *et al.* [1997]
- 1G10: Bound Rev in indirect immunofluorescence and also detected Rev in WB – used to detect localization of Rev throughout the cell. Kalland *et al.* [1994a]

No. 310
MAb ID 1G7
HXB2 Location Rev (96–105)
Author Location Rev (95–105)
Epitope GVGSPQILVE
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) mouse (IgG2bκ)
References Jensen *et al.* 1997; Kalland *et al.* 1994a

- 1G7: Peptide interaction mapped to aa 91-105, 96-110 – protein footprint to aa 95-105. Jensen *et al.* [1997]
- 1G7: Worked in indirect immunofluorescence and also detected Rev in WB – used to detect localization of Rev throughout the cell. Kalland *et al.* [1994a]

No. 311
MAb ID Ab3
HXB2 Location Rev (102–116)
Author Location Rev (102–116 BRU)
Epitope ILVESPTVLESDKTE
Neutralizing
Immunogen Vaccine

Vector/Type: protein *HIV component:* Rev
Species (Isotype) (IgG1)
Research Contact Tony Lowe and Jonathan Karn, MRC, Cambridge
References Henderson & Percipalle 1997

- Ab3: This binding site is at the carboxy end of Rev – Ab3 binding was not blocked by bound HIV RNA. Henderson & Percipalle [1997]

No. 312
MAb ID 2G2
HXB2 Location Rev
Author Location Rev
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Rev
Species (Isotype) mouse (IgG1κ)
References Orsini *et al.* 1995

- 2G2: Does not bind to any of a set of glutathione S-transferase (GST) Rev fusion proteins, or to Rev in a RIPA buffer, suggesting a conformational epitope. Orsini *et al.* [1995]

IV-C-15 gp160 Antibodies

No. 313
MAb ID M85
HXB2 Location gp160 (30–51)
Author Location gp120 (30–51 LAI)
Epitope ATEKLWVTVYYGVPVWKEATTT
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG1)
Ab Type C1
Research Contact Fulvia di Marzo Veronese
References Wyatt *et al.* 1997; Ditzel *et al.* 1997; Moore & Sodroski 1996; Moore *et al.* 1994d; Moore *et al.* 1994c; di Marzo Veronese *et al.* 1992

- M85: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding. Wyatt *et al.* [1997]
- M85: Binding inhibited by MAb 4D4#85, enhanced by conformationally sensitive anti-V3 MAb 5G11, and some anti-18 MAbs. Moore & Sodroski [1996]
- M85: C1 domain – mutation 40 Y/D impairs binding – the relative affinity for denatured/native gp120 is < .01, suggesting conformational component. Moore *et al.* [1994c]
- M85: Immunoblot and RIP reactive for strains IIIB, 451, MN, RF, and RUTZ – binds deglycosylated gp120. di Marzo Veronese *et al.* [1992]

No. 314
MAb ID 7E2/4
HXB2 Location gp160 (31–50)
Author Location gp120 (31–50 LAI)
Epitope TEKLWVTVYYGVPVWKEATT
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact S. Ranjbar, NIBSC, UK
References Maksiutov *et al.* 2002; Moore *et al.* 1994c

- 7E2/4: UK Medical Research Council AIDS reagent: ARP3050.
- 7E2/4: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF. Maksiutov *et al.* [2002]
- 7E2/4: C1 domain – the relative affinity for denatured/native gp120 is .07, suggesting conformational component. Moore *et al.* [1994c]

No. 315
MAb ID 4D4#85
HXB2 Location gp160 (41–50)
Author Location gp120 (LAI)
Epitope GVPVWKEATT
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact S. Nigida and L. Arthur, NCI, Frederick, MD USA
References Maksiutov *et al.* 2002; Binley *et al.* 1998; Wyatt *et al.* 1997; Moore & Sodroski 1996; Moore *et al.* 1994d; Moore *et al.* 1994c

- 4D4#85: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF. Maksiutov *et al.* [2002]
- 4D4#85: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- 4D4#85: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-50, are deleted. Wyatt *et al.* [1997]
- 4D4#85: Inhibits binding of C1 MAb M85, C1-C5 discontinuous epitope MAbs 181 and 212A, and CD4 binding induced MAbs 48d and 17b. Moore & Sodroski [1996]
- 4D4#85: C1 domain – the relative affinity, denatured/native gp120 is 0.1 – mutation 45 W/S impairs binding. Moore *et al.* [1994c]

No. 316
MAb ID M92
HXB2 Location gp160 (41–50)
Author Location gp120 (31–50 LAI)
Epitope GVPVWKEATT

Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) rat (IgG1)
Ab Type C1
Research Contact Fulvia di Marzo Veronese
References Maksiutov *et al.* 2002; Moore *et al.* 1994d; Moore *et al.* 1994c; di Marzo Veronese *et al.* 1992

- M92: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF. Maksiutov *et al.* [2002]
- M92: The relative affinity for denatured/native gp120 is 1. Moore *et al.* [1994c]
- M92: Immunoblot reactive, RIP negative, but precipitates deglycosylated gp120 – reacts with strains IIIB, 451, MN, RF, and RUTZ. di Marzo Veronese *et al.* [1992]

No. 317
MAb ID M86
HXB2 Location gp160 (42–61)
Author Location gp120 (42–61 LAI)
Epitope VPVWKEATTTLFCASDAKAY
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG1)
Ab Type C1
Research Contact Fulvia di Marzo Veronese
References Maksiutov *et al.* 2002; Moore *et al.* 1994c; di Marzo Veronese *et al.* 1992

- M86: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF. Maksiutov *et al.* [2002]
- M86: C1 domain – the relative affinity for denatured/native gp120 is 1. Moore *et al.* [1994c]
- M86: Immunoblot and RIP reactive for strains IIIB, 451, MN, RF, and RUTZ – binds deglycosylated gp120. di Marzo Veronese *et al.* [1992]

No. 318
MAb ID polyclonal
HXB2 Location gp160 (52–71)
Author Location Env (42–61 LAI)
Epitope LFCASDAKAYDTEVHNVWAT
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* Env
Species (Isotype) mouse
Ab Type C1
References Collado *et al.* 2000

- Vaccinia p14 can elicit NAbs and p39 tends to be immunodominant, so these two proteins were fused to regions of HIV-1 Env – reduced glycosylation was noted when p14 or p39 was placed in the N-term region of the fusion protein – chimeric proteins shifted the Env Ab response from V3 to either a C1 or C4 domain, depending on the construct – all chimeric Env proteins: 14kEnv, 39kEnv, and Env39k elicited a strong Ab response to the C1 region of gp120 (LFCASDAKAYDTEVHNVWAT), and Env39k mounted a strong response to the C4 region (KAMYAPPISGQIRCSSNITG) Collado *et al.* [2000]

No. 319
MAb ID 133/237
HXB2 Location gp160 (61–70)
Author Location gp120 (51–70 LAI)
Epitope YDTEVHNVWA
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C1
References Moore *et al.* 1994d; Moore *et al.* 1994c; Niedrig *et al.* 1992b

- 133/237: The relative affinity, denatured/native gp120 is 1.4 – mutation of position 69 W/L impairs binding. Moore *et al.* [1994c]
- 133/237: Region of overlap for reactive peptides is WATHA – weak neutralization of lab strains. Niedrig *et al.* [1992b]

No. 320
MAb ID 133/290
HXB2 Location gp160 (61–70)
Author Location gp120 (61–70 LAI)
Epitope YDTEVHNVWA
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C1
Research Contact M. Niedrig
References Pantophlet *et al.* 2003b; Yang *et al.* 2000; Binley *et al.* 1998; Wyatt *et al.* 1997; Binley *et al.* 1997a; Moore & Sodroski 1996; Wyatt *et al.* 1995; Moore *et al.* 1994d; Moore *et al.* 1994c; Thali *et al.* 1993; Niedrig *et al.* 1992b
Keywords vaccine antigen design

- 133/290: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- 133/290: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32,

522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000]
- 133/290: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- 133/290: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding. Wyatt *et al.* [1997]
- 133/290: Reciprocal binding inhibition with the antibody 522-149, that binds to a discontinuous epitope – binding is enhanced by some C5 and C1 binding site antibodies. Moore & Sodroski [1996]
- 133/290: Used for antigen capture assay, either to bind gp120 to the ELISA plate, or to quantify bound gp120. Wyatt *et al.* [1995]
- 133/290: The relative affinity for denatured/native gp120 is 2.2 – mutation in position 69 W/L impairs binding. Moore *et al.* [1994c]
- 133/290: Region of overlap for reactive peptides is WATHA – weak neutralization of lab strains. Niedrig *et al.* [1992b]

No. 321
MAb ID 133/11
HXB2 Location gp160 (64–78)
Author Location gp120 (64–78)
Epitope EVHNVWATHACVPTD
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp120
Species (Isotype) mouse (IgG1)
Ab Type C1
References Niedrig *et al.* 1992b

- 133/11: Region of overlap for reactive peptides is WATHA – weak neutralization of lab strains. Niedrig *et al.* [1992b]

No. 322
MAb ID D/3G5
HXB2 Location gp160 (73–82)
Author Location gp120 (73–82 LAI)
Epitope ACVPTDPNPQ
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp120
Species (Isotype) mouse (IgG1)
Ab Type C1
References Bristow *et al.* 1994

- D/3G5: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. Bristow *et al.* [1994]

No. 323
MAb ID D/6A11
HXB2 Location gp160 (73–82)
Author Location gp120 (73–82 LAI)
Epitope ACVPTDPNPQ
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp120
Species (Isotype) mouse
Ab Type C1
References Bristow *et al.* 1994

- D/6A11: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. Bristow *et al.* [1994]

No. 324
MAb ID D/5E12
HXB2 Location gp160 (73–92)
Author Location gp120 (73–92 LAI)
Epitope ACVPTDPNPQEVVLVNVTEN
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp120
Species (Isotype) mouse
Ab Type C1
References Bristow *et al.* 1994

- D/5E12: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. Bristow *et al.* [1994]

No. 325
MAb ID L5.1
HXB2 Location gp160 (79–93)
Author Location gp120 (89–103 IIIB)
Epitope PNPQEVVLVNVTENF
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: gp160
Species (Isotype) mouse (IgG)
Ab Type C1
References Akerblom *et al.* 1990

No. 326
MAb ID 4A7C6
HXB2 Location gp160 (81–90)
Author Location gp120 (81–90 LAI)
Epitope PQEVVLVNVT
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact R. Tedder

References Moore & Sodroski 1996; Moore *et al.* 1994d; Moore *et al.* 1994c; Moore & Ho 1993; Thali *et al.* 1993; Thiriart *et al.* 1989

- 4A7C6: UK Medical Research Council AIDS reagent: ARP 360.
- 4A7C6: Reciprocal binding inhibition with the antibody 133/192 – enhanced by anti-C5 antibodies, and C1 antibody 135/9. Moore & Sodroski [1996]
- 4A7C6: The relative affinity for denatured/native gp120 is 7.9 – mutation 88 N/P impairs binding. Moore *et al.* [1994c]
- 4A7C6: C1 region epitope (88 N/P substitutions abrogates binding), but substitutions 380 G/F and 420 I/R also impaired binding. Moore *et al.* [1994d]
- 4A7C6: Bound preferentially to denatured IIIB gp120. Moore & Ho [1993]

No. 327
MAb ID 1D10
HXB2 Location gp160 (81–100)
Author Location gp120 (81–100 LAI)
Epitope PQEVVLVNVTENFDMWKNDM
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) rat
Ab Type C1
References Moore *et al.* 1994c; Nakamura *et al.* 1992; Berman *et al.* 1991; Dowbenko *et al.* 1988

- 1D10: The relative affinity for denatured/native gp120 is 13 – mutation 88 N/P impairs binding. Moore *et al.* [1994c]
- 1D10: Cross-blocks 5B3 in IIIB-rsgp160 ELISA – type specific in rgp120 ELISA binding. Nakamura *et al.* [1992]

No. 328
MAb ID B242
HXB2 Location gp160 (83–92)
Author Location gp120 (83–92 LAI)
Epitope EVVLVNVTEN
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* gp160
Species (Isotype) mouse (IgG1)
Ab Type C1
References Bristow *et al.* 1994

- B242: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. Bristow *et al.* [1994]

No. 329
MAb ID 133/192
HXB2 Location gp160 (91–100)
Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C1
Research Contact Matthias Niedrig
References Pantophlet *et al.* 2003b; Binley *et al.* 1998; Binley *et al.* 1997a; Trkola *et al.* 1996a; Moore & Sodroski 1996; Moore *et al.* 1994d; Moore *et al.* 1994c; Moore *et al.* 1993b; Niedrig *et al.* 1992b
Keywords vaccine antigen design

- 133/192: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- 133/192: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- 133/192: Reciprocal binding inhibition with the antibody 4A7C6 – enhanced by some anti-C5 and-C1 antibodies. Moore & Sodroski [1996]
- 133/192: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]
- 133/192: The relative affinity for denatured/native gp120 is 1.8. Moore *et al.* [1994c]
- 133/192: C1 region – substitutions 76P/Y, 113 D/A or R, 117 K/W, 420 I/R, 427 W/S impair binding, other substitutions enhanced binding. Moore *et al.* [1994d]
- 133/192: Epitope seems complex, binds multiple peptides – weak neutralization of lab strain. Niedrig *et al.* [1992b]

No. 330
MAb ID 489.1(961)
HXB2 Location gp160 (91–100)
Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact C. Bruck, SKB, Belgium
References Moore *et al.* 1994c

- 489.1(961): NIH AIDS Research and Reference Reagent Program: 961.
- 489.1(961): The relative affinity for denatured/native gp120 is 1. Moore *et al.* [1994c]

No. 331
MAb ID 5B3
HXB2 Location gp160 (91–100)

Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp160
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Beretta & Dalgleish 1994; Nakamura *et al.* 1992; Berman *et al.* 1991

- 5B3: The relative affinity of denatured/native gp120 is 8.3. Moore *et al.* [1994c]
- 5B3: Cross-blocks 1D10 in competitive IIIB-rsgp160 ELISA – no neutralization – blocks IIIB-gp120 sCD4 binding – localized binding to residues 72-106. Nakamura *et al.* [1992]
- 5B3: Blocks gp120 -CD4 binding. Berman *et al.* [1991]

No. 332
MAb ID B10
HXB2 Location gp160 (91–100)
Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG1)
Ab Type C1
References Moore *et al.* 1994c; Abacioglu *et al.* 1994

- B10: There is FNM/FDM polymorphism in LAI-based peptides, and N is essential (J. P. Moore, per. comm.)
- B10: C1 region – epitope boundaries mapped by peptide scanning, FNMW core. Abacioglu *et al.* [1994]
- B10: The relative affinity for denatured/native gp120 is 0.4. Moore *et al.* [1994c]

No. 333
MAb ID B2
HXB2 Location gp160 (91–100)
Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG2b)
Ab Type C1
References Binley *et al.* 1997a; Moore *et al.* 1994d; Moore *et al.* 1994c; Abacioglu *et al.* 1994; Thali *et al.* 1993

- B2: There is FNM/FDM polymorphism in LAI-based peptides, and N is essential (J. P. Moore, per. comm.)
- B2: C1 region – epitope boundaries mapped by peptide scanning, FNMW core. Abacioglu *et al.* [1994]
- B2: The relative affinity for denatured/native gp120 is 1.4. Moore *et al.* [1994c]

No. 334
MAb ID C6 (Ch6)
HXB2 Location gp160 (91–100)
Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG1)
Ab Type C1
References Pincus *et al.* 1996; Moore *et al.* 1994c; Abacioglu *et al.* 1994; Pincus & McClure 1993

- C6: There is FNM/FDM polymorphism in LAI-based peptides – N is essential (J. P. Moore, per. comm.)
- C6: NIH AIDS Research and Reference Reagent Program: 810.
- C6: Called Ch6 – binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect. Pincus & McClure [1993]; Pincus *et al.* [1996]
- C6: C1 region – epitope boundaries mapped by peptide scanning, FNMW core. Abacioglu *et al.* [1994]
- C6: The relative affinity for denatured/native gp120 is 0.9. Moore *et al.* [1994c]

No. 335
MAb ID MF49.1
HXB2 Location gp160 (91–100)
Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- MF49.1: The relative affinity of denatured/native gp120 is 3.8. Moore *et al.* [1994c]

No. 336
MAb ID T1.1
HXB2 Location gp160 (91–100)
Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* gp160
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Broliden *et al.* 1990; Akerblom *et al.* 1990

- T1.1: C1 region – the relative affinity for denatured/native gp120 is 1. Moore *et al.* [1994c]
- T1.1: Also reacted in solid phase with gp120(234-248) NGTGPCTNVSTQCT. Akerblom *et al.* [1990]

• T1.1: No ADCC activity – reactive peptide: NVTENFNMWKNDMVEQ, IIIB. Broliden *et al.* [1990]

No. 337
MAb ID T7.1
HXB2 Location gp160 (91–100)
Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994d; Moore *et al.* 1994c; Bolmstedt *et al.* 1990; Akerblom *et al.* 1990

• T7.1: The relative affinity of denatured/native gp120 is 4.0. Moore *et al.* [1994c]

No. 338
MAb ID T9
HXB2 Location gp160 (91–100)
Author Location gp120 (91–100 LAI)
Epitope ENFDMWKNDM
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact Lennart Akerblom, Britta Wahren and Jorma Hinkula
References Binley *et al.* 1997a; Moore *et al.* 1994d; Moore *et al.* 1994c; Bolmstedt *et al.* 1990; Akerblom *et al.* 1990

• T9: There are two HIV-Abs with the name T9, one binds to gp41, one to gp120.
• T9: The relative affinity of denatured/native gp120 is 7.9. Moore *et al.* [1994c]
• T9: Binds to the C1 region – 45 W/S, 88 N/P, 256 S/Y, 262 N/T, 475 M/S, 485 1.83, and 491 I/F enhanced binding, no substitution tested significantly inhibited. Moore *et al.* [1994d]

No. 339
MAb ID GV4D3
HXB2 Location gp160 (92–100)
Author Location gp120 (92–100 IIIB)
Epitope NFNMWKNDM
Neutralizing
Immunogen Vaccine
Vector/Type: protein-Ab complex *HIV component:* gp120-Mab complex
Species (Isotype) mouse
Ab Type C1
Research Contact Patricia Earl and Christopher Broder, NIH
References Denisova *et al.* 1996

• GV4D3: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes – MAbs GV4H4 and GV5F9 are homologous to GV4D3 and were generated in the same experiment. Denisova *et al.* [1996]

No. 340
MAb ID B27
HXB2 Location gp160 (93–96)
Author Location gp120 (94–97 BH10)
Epitope FNMW
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* gp160
Species (Isotype) mouse (IgG1)
Ab Type C1
References Bristow *et al.* 1994; Abacioglu *et al.* 1994

• B27: C1 region – epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]
• B27: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. Bristow *et al.* [1994]

No. 341
MAb ID B9
HXB2 Location gp160 (93–96)
Author Location gp120 (93–96 LAI)
Epitope FNMW
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG1)
Ab Type C1
References Abacioglu *et al.* 1994

• B9: Binds C1 region – epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 342
MAb ID B35
HXB2 Location gp160 (93–98)
Author Location gp120 (94–99 BH10)
Epitope FNMWKN
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG1)
Ab Type C1
References Abacioglu *et al.* 1994

• B35: C1 region – epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 343
MAb ID D/4B5
HXB2 Location gp160 (93–101)
Author Location gp120 (93–101 LAI)
Epitope FNMWKNDMV

Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp120
Species (Isotype) mouse
Ab Type C1
References Bristow *et al.* 1994

- D/4B5: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. Bristow *et al.* [1994]

No. 344
MAb ID D/5A11
HXB2 Location gp160 (93–101)
Author Location gp120 (93–101 LAI)
Epitope FNMWKNDMV
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp120
Species (Isotype) mouse
Ab Type C1
References Bristow *et al.* 1994

- D/5A11: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. Bristow *et al.* [1994]

No. 345
MAb ID D/6B2
HXB2 Location gp160 (93–101)
Author Location gp120 (93–101 LAI)
Epitope FNMWKNDMV
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp120
Species (Isotype) mouse (IgG1)
Ab Type C1
References Bristow *et al.* 1994

- D/6B2: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. Bristow *et al.* [1994]

No. 346
MAb ID B18
HXB2 Location gp160 (101–110)
Author Location gp120 (101–110 LAI)
Epitope VEQMHEDIIS
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG2a)
Ab Type C1
References Moore *et al.* 1994c; Abacioglu *et al.* 1994

- B18: C1 region – epitope boundaries mapped by peptide scanning, HEDII core. Abacioglu *et al.* [1994]
- B18: The relative affinity for denatured/native gp120 is 1. Moore *et al.* [1994c]

No. 347
MAb ID B20
HXB2 Location gp160 (101–110)
Author Location gp120 (101–110 LAI)
Epitope VEQMHEDIIS
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG2a)
Ab Type C1
References Moore *et al.* 1994c; Abacioglu *et al.* 1994

- B20: C1 region – epitope boundaries mapped by peptide scanning – HEDII core. Abacioglu *et al.* [1994]
- B20: The relative affinity for denatured/native gp120 is 1. Moore *et al.* [1994c]

No. 348
MAb ID MF39.1 (39.1)
HXB2 Location gp160 (101–110)
Author Location gp120 (101–110 LAI)
Epitope VEQMHEDIIS
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Cook *et al.* 1994; Thiriart *et al.* 1989

- MF39.1: Called 39.1, and is probably the same as MF39.1 – MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. Cook *et al.* [1994]
- MF39.1: The relative affinity of denatured/native gp120 is 30. Moore *et al.* [1994c]

No. 349
MAb ID 187.2.1 (187.1)
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact Claudine Bruck and Clothilde Thiriart
References Moore *et al.* 1994d; Moore *et al.* 1994c; Cook *et al.* 1994; Moore & Ho 1993; Thiriart *et al.* 1989

- 187.2.1: UK Medical Research Council AIDS reagent: ARP332.
- 187.2.1: Called 187.1, and is probably the same as 187.2.1 – MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. Cook *et al.* [1994]
- 187.2.1: The relative affinity for denatured/native gp120 is 7 – mutations 113 D/A (not D/R) and 117 K/W impair binding. Moore *et al.* [1994c]
- 187.2.1: Called 187.1, and is probably the same as 187.2.1 – bound preferentially to denatured IIIB gp120. Moore & Ho [1993]

No. 350
MAb ID 37.1.1(ARP 327) (37.1)
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact Claudine Bruck
References Moore *et al.* 1994c; Moore & Ho 1993; Thiriart *et al.* 1989

- 37.1.1: UK Medical Research Council AIDS reagent: ARP327.
- 37.1.1: The relative affinity for denatured/native gp120 is 8.6 – mutations 113 D/R (not D/A) and 117 K/W impair binding. Moore *et al.* [1994c]
- 37.1.1: Called 37.1 – bound preferentially to denatured IIIB gp120. Moore & Ho [1993]

No. 351
MAb ID 6D8
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) rat
Ab Type C1
References Moore *et al.* 1994c; Nakamura *et al.* 1992; Dowbenko *et al.* 1988

- 6D8: The relative affinity for denatured/native gp120 is 15 – mutations 113 D/R and 113 D/A impair binding. Moore *et al.* [1994c]
- 6D8: Highly cross reactive with multiple stains by rgp120 ELISA. Nakamura *et al.* [1992]

No. 352
MAb ID M96
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) rat (IgG2a)
Ab Type C1
Research Contact Fulvia di Marzo Veronese
References Moore *et al.* 1994d; Moore *et al.* 1994c; di Marzo Veronese *et al.* 1992

- M96: C1 region – the relative affinity for denatured/native gp120 is 6. Moore *et al.* [1994c]
- M96: Immunoblot reactive for strains IIIB, 451, MN, RF, and RUTZ. di Marzo Veronese *et al.* [1992]

No. 353
MAb ID MF119.1
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- MF119.1: The relative affinity for denatured/native gp120 is 30 – mutations 113 D/A, 113 D/R, and 117 K/W impair binding. Moore *et al.* [1994c]

No. 354
MAb ID MF4.1
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- MF4.1: The relative affinity for denatured/native gp120 is 8. Moore *et al.* [1994c]

No. 355
MAb ID MF53.1
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- MF53.1: The relative affinity for denatured/native gp120 is 10. Moore *et al.* [1994c]

No. 356
MAb ID MF58.1
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

No. 357
MAb ID MF77.1
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- MF77.1: The relative affinity for denatured/native gp120 is 11. Moore *et al.* [1994c]

No. 358
MAb ID T2.1
HXB2 Location gp160 (101–120)
Author Location gp120 (101–120 LAI)
Epitope VEQMHEDIISLWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact Lennart Akerblom, Britta Wahren and Jorma Hinkula
References Moore *et al.* 1994d; Moore *et al.* 1994c; Bolmstedt *et al.* 1990; Akerblom *et al.* 1990

- T2.1: The relative affinity for denatured/native gp120 is .27 – mutations 113 D/R, 106 E/A, and 117 D/A impair binding. Moore *et al.* [1994c]

No. 359
MAb ID 11/65 (11/65a/5h)
HXB2 Location gp160 (102–121)
Author Location gp120 (311–321 HXB10)
Epitope EQMHEDIISLWDQSLKPCVK
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10 *HIV component:* gp120
Species (Isotype) rat (IgG2b)
Ab Type C1
References Peet *et al.* 1998; McKeating *et al.* 1993b; McKeating *et al.* 1992a

- 11/65: UK Medical Research Council AIDS reagent: ARP3076.
- 11/65: Called 11/65a/5h – The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/65 was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]
- 11/65: Binds only soluble gp120, not virion bound – used to quantify gp120 shedding – (numbering is incorrect in original?) McKeating *et al.* [1992a]

No. 360
MAb ID W1
HXB2 Location gp160 (102–121)
Author Location gp120 (102–121 LAI)
Epitope EQMHEDIISLWDQSLKPCVK
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact D. Weiner, U. Penn.
References Moore *et al.* 1994c

- W1: The relative affinity for denatured/native gp120 is 6 – mutations 113 D/A, 113 D/R, and 117 K/W impair binding. Moore *et al.* [1994c]

No. 361
MAb ID T11
HXB2 Location gp160 (102–125)
Author Location gp120 (102–125)
Epitope EQMHEDIISLWDQSLKPCVKLTPL
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* oligomeric gp140
Species (Isotype) mouse
Ab Type C1
Research Contact R. Doms, Univ. of Pennsylvania
References Jagodzinski *et al.* 1996; Earl *et al.* 1994

- T11: The sulfated polysaccharide, curdlan sulfate (CRDS), binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop from gp120 results in more potent T11 inhibition by CRDS. Jagodzinski *et al.* [1996]
- T11: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 362
MAb ID GV1A8
HXB2 Location gp160 (105–113)
Author Location gp120 (105–113 IIIB)
Epitope HEDIISLWD
Neutralizing
Immunogen Vaccine

Vector/Type: protein-Ab complex *HIV component:* gp120-Mab complex
Species (Isotype) mouse
Ab Type C1
References Denisova *et al.* 1996

- GV1A8: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes – MAbs GV7A4 and GV5H5 are homologous to GV1A8 and were generated in the same experiment. Denisova *et al.* [1996]

No. 363
MAb ID 11
HXB2 Location gp160 (111–120)
Author Location gp120 (101–120 LAI)
Epitope LWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- 11: The relative affinity for denatured/native gp120 is 7.8 – mutation 113 D/R impairs binding. Moore *et al.* [1994c]

No. 364
MAb ID 12G10
HXB2 Location gp160 (111–120)
Author Location gp120 (101–120 LAI)
Epitope LWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- 12G10: The relative affinity for denatured/native gp120 is 17 – mutation 117 K/W impairs binding. Moore *et al.* [1994c]

No. 365
MAb ID 135/9 (87-135/9)
HXB2 Location gp160 (111–120)
Author Location gp120 (111–120 LAI)
Epitope LWDQSLKPCV
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C1
Research Contact Matthias Niedrig
References Yang *et al.* 2000; Kropelin *et al.* 1998; Binley *et al.* 1998; Binley *et al.* 1997a; Trkola *et al.* 1996a; Moore & Sodroski 1996; Moore *et al.* 1994d; Moore *et al.* 1994c; Niedrig *et al.* 1992b

- 135/9: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000]
- 135/9: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- 135/9: Noted to bind to C1 peptide HEDIISLWDQSLK – blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) Kropelin *et al.* [1998]
- 135/9: Binding is enhanced by some anti-C1 and anti-C5 antibodies – enhances binding of some anti-V3, anti-C4 and anti-V2 MAbs – 135/9 binds to predicted alpha-helix in C1. Moore & Sodroski [1996]
- 135/9: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]
- 135/9: The relative affinity for denatured/native gp120 is 15 – mutation 113 D/R impairs binding to native and denatured, 113 D/A only to denatured. Moore *et al.* [1994c]
- 135/9: Substitutions 106 E/A, 113 D/A or R, and 117 K/W impair binding, some substitutions enhance binding. Moore *et al.* [1994d]
- 135/9: Defines the epitope as gp120(114-123) MHEDIISLWD (core LWD?) – weak neutralization of lab strain. Niedrig *et al.* [1992b]

No. 366
MAb ID 7C10
HXB2 Location gp160 (111–120)
Author Location gp120 (101–120 LAI)
Epitope LWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- 7C10: The relative affinity for denatured/native gp120 is 5.8 – mutation 117 K/W impairs binding. Moore *et al.* [1994c]

No. 367
MAb ID C4
HXB2 Location gp160 (111–120)
Author Location gp120 (101–120 LAI)
Epitope LWDQSLKPCV
Subtype B

Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG1)
Ab Type C1
Research Contact George Lewis
References Moore *et al.* 1994c; Moore & Ho 1993; Abacioglu *et al.* 1994

- C4: C1 region – epitope boundaries mapped by peptide scanning, BH10 core IISLW. Abacioglu *et al.* [1994]
- C4: The relative affinity for denatured/native gp120 is 10. Moore *et al.* [1994c]
- C4: Bound preferentially to denatured IIIB gp120. Moore & Ho [1993]

No. 368
MAb ID MF46.1
HXB2 Location gp160 (111–120)
Author Location gp120 (101–120 LAI)
Epitope LWDQSLKPCV
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C1
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- MF46.1: The relative affinity for denatured/native gp120 is 8.5. Moore *et al.* [1994c]

No. 369
MAb ID 6D5
HXB2 Location gp160 (122–141)
Author Location gp120 (122–141 LAI)
Epitope LTPLCVSLKCTDLKNDTNTN
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type V2
Research Contact S. Nigida and L. Arthur, NCI, Frederick, MD USA
References Moore *et al.* 1994d; Moore *et al.* 1994c

- 6D5: The relative affinity for denatured/native gp120 is 15 – mutations Delta119-205 and 125 L/G impair binding. Moore *et al.* [1994c]

No. 370
MAb ID B33
HXB2 Location gp160 (123–142)
Author Location gp120 (123–142 LAI)
Epitope TPLCVSLKCTDLGNATNTNS
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* gp160
Species (Isotype) mouse (IgG2bκ)
Ab Type V2
Research Contact Daniels
References Bristow *et al.* 1994; Abacioglu *et al.* 1994

- B33: UK Medical Research Council AIDS reagent: ARP304, gp160/41 binding.
- B33: There are two MAbs in the literature named B33, see also gp160(727-734) Abacioglu *et al.* [1994]
- B33: Epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]
- B27: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. Bristow *et al.* [1994]

No. 371
MAb ID polyclonal (VEI1)
HXB2 Location gp160 (131–151)
Author Location Env (131–151)
Epitope CTDLKNDTNTNSSSGRMMMEK
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Carlos *et al.* 1999

- Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ. Carlos *et al.* [1999]

No. 372
MAb ID 35D10/D2
HXB2 Location gp160 (139–155)
Author Location gp120
Epitope NTKSSNWKEMDGEIK
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 35D10/D2: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)

- 35D10/D2: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 373
MAb ID 40H2/C7
HXB2 Location gp160 (139–155)
Author Location gp120
Epitope NTKSSNWKEMDGEIK
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 40H2/C7: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 40H2/C7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 374
MAb ID 43A3/E4
HXB2 Location gp160 (139–155)
Author Location gp120
Epitope NTKSSNWKEMDGEIK
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 43A3/E4: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 43A3/E4: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 375
MAb ID 43C7/B9
HXB2 Location gp160 (139–155)
Author Location gp120
Epitope NTKSSNWKEMDGEIK
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 43C7/B9: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 43C7/B9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were

highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 376
MAb ID 45D1/B7
HXB2 Location gp160 (139–155)
Author Location gp120
Epitope NTKSSNWKEMDGEIK
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 45D1/B7: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 45D1/B7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 377
MAb ID 46E3/E6
HXB2 Location gp160 (139–155)
Author Location gp120
Epitope NTKSSNWKEMDGEIK
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 46E3/E6: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 46E3/E6: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 378
MAb ID 58E1/B3
HXB2 Location gp160 (139–155)
Author Location gp120
Epitope NTKSSNWKEMDGEIK
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 58E1/B3: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 58E1/B3: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 379
MAb ID 64B9/A6
HXB2 Location gp160 (139–155)
Author Location gp120

Epitope NTKSSNWKEMDGEIK
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162
HIV component: gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 64B9/A6: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 64B9/A6: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 380
MAb ID 69D2/A1
HXB2 Location gp160 (139–155)
Author Location gp120
Epitope NTKSSNWKEMDGEIK
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162
HIV component: gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 69D2/A1: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 69D2/A1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 381
MAb ID 82D3/C3
HXB2 Location gp160 (139–155)
Author Location gp120
Epitope NTKSSNWKEMDGEIK
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162
HIV component: gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V1
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 82D3/C3: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 82D3/C3: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 382
MAb ID 2H1B
HXB2 Location gp160 (155–161)
Author Location gp120 (370–376 HIV2ROD)
Epitope RNISFKA
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* HIV-2 ROD
Species (Isotype) mouse
Ab Type C3
References Matsushita *et al.* 1995

- 2H1B: Binds in WB, but binds poorly to Env on the cell surface. Matsushita *et al.* [1995]

No. 383
MAb ID 697-D (697D, 697-30D)
HXB2 Location gp160 (161–180)
Author Location gp120 (161–180 IIIB)
Epitope ISTSIRGKVQKEYAFFYKLD
Neutralizing P (weak)
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V2
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) or Cellular Products Inc, Buffalo NY
References Gorny & Zolla-Pazner 2004; He *et al.* 2002; Maksiutov *et al.* 2002; Edwards *et al.* 2002; Nyambi *et al.* 2000; Hioe *et al.* 2000; Gorny *et al.* 2000; Stamatatos & Cheng-Mayer 1998; Nyambi *et al.* 1998; Parren *et al.* 1997b; Fouts *et al.* 1997; Binley *et al.* 1997a; Trkola *et al.* 1996a; Moore & Ho 1995; Forthal *et al.* 1995; Gorny *et al.* 1994
Keywords ADCC, antibody binding site definition and exposure, co-receptor, enhancing activity, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 697-D: In a review of Envelope binding MAbs in this database, V2-specific MAbs are noted to have some ability to neutralize HIV-1, but generally weak with limited cross-reactivity; it weakly neutralizes some primary but not TCLA strains. 697-D is the best characterized of the anti-V2 MAbs, and binds weakly and sporadically to isolates from clades A-D. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**)
- 697-D: Called 697D – Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. Edwards *et al.* [2002] (**antibody binding site definition and exposure**)
- 697-D: Called 697D – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A, 4117C and 697D were used as controls. He *et al.* [2002]
- 697-D: This epitope is similar to a fragment of the human protein macrophage colony stimulating factor I receptor SISIRLKVQK. Maksiutov *et al.* [2002]
- 697-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)
- 697-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – V2 MAb 697-D did not effect proliferation. Hioe *et al.* [2000]
- 697-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 697-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind weakly with a similar pattern of specificity to virions, and bound well to soluble gp120: weak binding to 1/4 B clade viruses (CA5), and weak binding to viruses from subtype A and D. Nyambi *et al.* [1998] (**inter-clade comparisons**)
- 697-D: Called 697-30D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V2 MAbs G3.4, G3.136, or 687-30D. Stamatatos & Cheng-Mayer [1998] (**variant cross-recognition or cross-neutralization**)
- 697-D: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 697-D bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- 697-D: Does not neutralize TCLA strains but neutralizes some primary isolates weakly. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 697-D: Partial inhibition of gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a] (**co-receptor**)
- 697-D: Not neutralizing, no ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995] (**ADCC**, **enhancing activity**)
- 697-D: Review: called 697/30D – neutralizes some primary, but not lab adapted strains. Moore & Ho [1995] (**variant cross-recognition or cross-neutralization**, **review**)
- 697-D: Conformational with weak reactivity to V2 peptide ISTSIRGKVQKEYAFFYKLD – neutralized 3/4 primary isolates, but none of 4 lab strains – V2 substitutions 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS abrogate binding – anti-C4 MAbs G3-536 and G45-60 enhance binding – mild oxidation of carbohydrate moieties inhibits binding. Gorny *et al.* [1994] (**antibody binding site definition and exposure**)

No. 384
MAb ID 6C4/S
HXB2 Location gp160 (162–169)
Author Location gp120 (BH10)

Epitope STSIRGKV
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype)
Research Contact S. Ranjbar (NIBSC, UK)
References Moore *et al.* 1993a

- 6C4/S: UK Medical Research Council AIDS reagent: ARP3049.

No. 385
MAb ID C108G
HXB2 Location gp160 (162–169)
Author Location gp120 (162–169 HXB2)
Epitope STSIRGKV
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) chimpanzee (IgG1κ)
Ab Type V2
Research Contact S. Tilley, Public Health Research Institute, NY, NY
References Gorny & Zolla-Pazner 2004; Alsmadi & Tilley 1998; Mondor *et al.* 1998; Ugolini *et al.* 1997; Warrier *et al.* 1996; Warrier *et al.* 1995; Wu *et al.* 1995; Warrier *et al.* 1994
Keywords ADCC, antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, review, variant cross-recognition or cross-neutralization

- C108G: This MAb is unusual among V2-directed MAbs. It is glycan dependent and can neutralize both a primary isolate (BaL and a TCLA (IIIB) strain. Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **review**)
- C108G: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – C108G bound and directed lysis against only IIIB – this is first demonstration of ADCC directed by a V2 specific MAb. Alsmadi & Tilley [1998] (**ADCC**, **variant cross-recognition or cross-neutralization**)
- C108G: Inhibits HX10 binding to both CD4 positive and negative HeLa cells. Mondor *et al.* [1998]
- C108G: Viral binding inhibition by C108G was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997] (**antibody binding site definition and exposure**)
- C108G: Synergistic neutralization of HIV-1 when combined with anti-V3 MAbs 0.5beta and C311E, or anti-CD4BS MAbs, 1125H and 5145A – neutralization further enhanced by presence of both 1125H and 0.5beta. Warrier *et al.* [1996] (**antibody interactions**)
- C108G: Characterization of MAb variable region. Warrier *et al.* [1995] (**antibody sequence, variable domain**)
- C108G: Strain specificity: LAI, BaL, HXB2 – conformational character – glycosylation site at 160 critical – mutation of conserved glycosylation site at 156 increased epitope exposure. Wu *et al.* [1995] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- C108G: Chimps were infected with HIV-1 IIIB, and this high affinity MAb gave potent neutralization of HIV-1 IIIB – binding not affected by reduction of disulfide bonds – binding disrupted by removal of N-linked glycans – peptide binds with lower affinity than glycosylated Env. Warrier *et al.* [1994] (**antibody binding site definition and exposure**, **antibody generation**)

No. 386
MAb ID 10/76b
HXB2 Location gp160 (162–170)
Author Location gp120 (162–171 BH10)
Epitope STSIRGKVQ
Neutralizing L (HXB10)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2a)
References McKeating *et al.* 1996; Wu *et al.* 1995; Shotton *et al.* 1995; McKeating *et al.* 1993a; McKeating *et al.* 1993b

- 10/76b: UK Medical Research Council AIDS reagent: ARP3077.
- 10/76b: Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. McKeating *et al.* [1996]
- 10/76b: Cross-competes with MAbs 10/76b and 11/4b – HXB2 neutralization escape mutant has the substitution I/T at residue 165. Shotton *et al.* [1995]
- 10/76b: Included in cross-competition and neutralization studies. Shotton *et al.* [1995]
- 10/76b: HX10 strain specificity – binds native, deglycosylated, or denatured gp120. Wu *et al.* [1995]
- 10/76b: R to L substitution abrogated binding – human sera recognize epitope. McKeating *et al.* [1993b]

No. 387
MAb ID 11/41e
HXB2 Location gp160 (162–170)
Author Location gp120 (162–171)
Epitope STSIRGKVQ
Neutralizing L (HXB10)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG1)
References Wu *et al.* 1995; Shotton *et al.* 1995; McKeating *et al.* 1993b

- 11/41e: Included in cross-competition and neutralization studies. Shotton *et al.* [1995]
- 11/41e: HX10 strain specificity – binds native and deglycosylated gp120. Wu *et al.* [1995]
- 11/41e: R to L abrogated binding – human sera recognize the epitope. McKeating *et al.* [1993b]

No. 388
MAb ID 11/4b
HXB2 Location gp160 (162–170)
Author Location gp120 (162–171)
Epitope STSIRGKVQ
Neutralizing L (HXB10)

Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2a)
References Moore & Sodroski 1996; Wu *et al.* 1995; Shotton *et al.* 1995; McKeating *et al.* 1993b

- 11/4b: Linear V2 epitope – reciprocal binding enhancement of anti-V2 discontinuous epitope antibodies (in contrast to BAT085) and CD4 inducible antibody 48d. Reciprocal inhibits BAT085 binding – inhibits CRA-3 binding CRA-3 does not inhibit 11/4b. Moore & Sodroski [1996]
- 11/4b: Cross-competes with MAbs 10/76b and 11/4c – HXB2 neutralization escape mutant has the substitution I/T at residue 165. Shotton *et al.* [1995]
- 11/4b: HXB10 strain specificity – binds native, deglycosylated, or denatured gp120. Wu *et al.* [1995]
- 11/4b: A change from R to L abrogated binding – human sera recognize epitope. McKeating *et al.* [1993b]

No. 389
MAb ID RSD-33
HXB2 Location gp160 (162–170)
Author Location gp120 (162–171)
Epitope STSIRGKVQ
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype)
Research Contact R. Daniels (NIMR, UK)
References Moore *et al.* 1993a

No. 390
MAb ID 11/4c (11/4c/1j/4j)
HXB2 Location gp160 (162–170)
Author Location gp120 (152–181)
Epitope STSIRGKVQ
Neutralizing L (HXB2)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2a)
Ab Type V2
References Peet *et al.* 1998; Shotton *et al.* 1995; Wu *et al.* 1995; McKeating *et al.* 1993b

- 11/4c: UK Medical Research Council AIDS reagent: ARP3035.
- 11/4c: Called 11/4c/1j/4j – The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/4c was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]
- 11/4c: Cross-competes with MAbs 10/76b and 11/4b – HXB2 neutralization escape mutant has the substitution I/T at residue 165. Shotton *et al.* [1995]
- 11/4c: HX10 strain specificity – binds native, deglycosylated, or denatured gp120. Wu *et al.* [1995]
- 11/4c: R to L substitution abrogated binding – human sera recognize epitope. McKeating *et al.* [1993b]

No. 391
MAb ID 8.22.2
HXB2 Location gp160 (162–178)
Author Location gp120
Epitope TTSIRDKVQKEYALFYK
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162
HIV component: gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V2
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Pinter *et al.* 2004; Gorny & Zolla-Pazner 2004; Maksiutov *et al.* 2002; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 8.22.2: This broad review of anti-Envelope MAbs notes that V2 MAbs are generally weakly neutralizing at best, and somewhat strain specific. 8.22.2 weakly neutralizes SF162. Gorny & Zolla-Pazner [2004] (**review**)
- 8.22.2: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype.Three anti-V2 MAb were tested – 8.22.2 weakly neutralized SF162, and did not neutralize JRFL at all. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 8.22.2 : Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – 8.22.2 was the only V2-specific MAb created and it could cross-compete with MAb 697D – 8.22.2 could cross-react with BaL and JR-FL, two B clade R5 strains, but not B clade X4 or E clade viruses, and it could weakly neutralize autologous strain SF162. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 8.22.2: This epitope is similar to a fragment of the human protein macrophage colony stimulating factor I receptor SISIRLKVQK. Maksiutov *et al.* [2002]

No. 392
MAb ID 12b
HXB2 Location gp160 (162–181)
Author Location gp120 (162–181)

Epitope STSIRGKVQKEYAFFYKLDI
Neutralizing L (HXB10)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2a)
Ab Type V2
References Maksiutov *et al.* 2002; McKeating *et al.* 1996; Shotton *et al.* 1995

- 12b: This epitope is similar to a fragment of the human protein macrophage colony stimulating factor I receptor SISIRLKVQK. Maksiutov *et al.* [2002]
- 12b: Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. McKeating *et al.* [1996]
- 12b: V2 MAb neutralized HXB2 – position 179-180 LD to DL abrogates binding – competes with 60b, but not 74. Shotton *et al.* [1995]

No. 393
MAb ID G3-136 (G3.136)
HXB2 Location gp160 (170–180)
Author Location gp120 (170–180 IIIB)
Epitope QKEYAFFYKLD
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp120
Species (Isotype) mouse (IgG)
Ab Type V2
Research Contact Tanox Biosystems Inc and David Ho, ADARC, NY
References Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Ly & Stamatatos 2000; Stamatatos & Cheng-Mayer 1998; Parren *et al.* 1998a; Wyatt *et al.* 1997; Ditzel *et al.* 1997; Stamatatos *et al.* 1997; Binley *et al.* 1997a; Poignard *et al.* 1996a; Moore & Sodroski 1996; Stamatatos & Cheng-Mayer 1995; Sattentau & Moore 1995; Yoshiyama *et al.* 1994; Moore *et al.* 1993a; Moore & Ho 1993; Thali *et al.* 1993; Pirofski *et al.* 1993; Fung *et al.* 1992
Keywords antibody interactions, vaccine antigen design

- G3-136: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- G3-136: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V2 MAb used. Zwick *et al.* [2003] (**antibody interactions**)
- G3-136: Called G3.136 – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. Ly & Stamatatos [2000]
- G3-136: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- G3-136: Called G3.136 – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V2 MAbs G3.4, G3.136, or 687-30D. Stamatatos & Cheng-Mayer [1998]
- G3-136: Called G3.136 – does not mediate gp120 virion dissociation in contrast to anti-V2 MAb G3-4 – not neutralizing for SF162 or SF128A in either primary macrophages or PBMC. Stamatatos *et al.* [1997]
- G3-136: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. Wyatt *et al.* [1997]
- G3-136: Described epitope as STSIRGKVKEYAFFYKLDI – binds oligomer – binding of V2 MAbs G3-136, G3-4 or BAT123 did not significantly alter gp120 dissociation from virus or expose the gp41 epitope of MAb 50-69, in contrast to anti-V3 MAbs. Poignard *et al.* [1996a]
- G3-136: Bound preferentially to the monomeric rather than oligomeric form of LAI gp120 – neutralizes cell free Hx10. Sattentau & Moore [1995]
- G3-136: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V2 loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a – anti-V2 MAbs G3-4 and G3.136 don't bind to T-cell tropic SF2. Stamatatos & Cheng-Mayer [1995]
- G3-136: HIV-1 RF V2 substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity. Yoshiyama *et al.* [1994]
- G3-136: Conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120, and does not inhibit HIV-1 sera from binding to IIIB gp120. Moore & Ho [1993]
- G3-136: Marginal binding to peptide, binding inhibited by 183/184 PI/SG substitution. Moore *et al.* [1993a]

- G3-136: Binding enhanced by selected antibodies to C1, C4, C5, V3 and anti-CD4 binding site MAbs – enhances binding of selected V3, C4 and anti-CD4 binding site MAbs. Moore *et al.* [1993a]
- G3-136: V2 region – binds and neutralizes IIIB and RF in CEM-SS cells, but not MN – neutralization activity against a few primary isolates in PBMC – sCD4 binding inhibits binding (contrast with BAT085) – deglycosylation or reduction of gp120 by DTT diminishes reactivity. Fung *et al.* [1992]

No. 394
MAb ID G3-4 (G3.4)
HXB2 Location gp160 (170–180)
Author Location gp120 (170–180 BH10)
Epitope QKEYAFFYKLD
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp120
Species (Isotype) mouse (IgG2bκ)
Ab Type V2
Research Contact Tanox Biosystems Inc and David Ho, ADARC, NY
References McCaffrey *et al.* 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Srivastava *et al.* 2002; Ly & Stamatatos 2000; Stamatatos & Cheng-Mayer 1998; Parren *et al.* 1998a; Wyatt *et al.* 1997; Ditzel *et al.* 1997; Stamatatos *et al.* 1997; Binley *et al.* 1997a; Poignard *et al.* 1996a; Moore & Sodroski 1996; Jagodzinski *et al.* 1996; Sattentau & Moore 1995; Wu *et al.* 1995; Stamatatos & Cheng-Mayer 1995; Yoshiyama *et al.* 1994; Thali *et al.* 1994; Gorny *et al.* 1994; Moore *et al.* 1994b; Moore *et al.* 1993a; Thali *et al.* 1993; Sattentau *et al.* 1993; Sullivan *et al.* 1993; Moore & Ho 1993; McKeating *et al.* 1992a; Fung *et al.* 1992; Ho *et al.* 1992; Ho *et al.* 1991a
Keywords antibody binding site definition and exposure, antibody interactions, vaccine antigen design

- G3-4: Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The SF2 and all five glycan mutants were resistant to G3-4. V3 glycans tended to shield V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans shielded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- G3-4: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- G3-4: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V2 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- G3-4: Called G3.4 – Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – G3.4 recognized o-gp140. Srivastava *et al.* [2002]
- G3-4: Called G3.4 – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. Ly & Stamatatos [2000]
- G3-4: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- G3-4: Called G3.4 – Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V2 MAbs G3.4, G3.136, or 687-30D. Stamatatos & Cheng-Mayer [1998]
- G3-4: Called G3.4 – mediates gp120 virion dissociation in contrast to anti-V2 MAb G3-136 – not neutralizing for SF162 or SF128A in either primary macrophages or PBMC. Stamatatos *et al.* [1997]
- G3-4: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. Wyatt *et al.* [1997]
- G3-4: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop from gp120 results in more potent G3-4 binding inhibition by CRDS – G3-4 epitope described as 176-184 FYKLDIIPI and 191-193 YSL. Jagodzinski *et al.* [1996]
- G3-4: Binding enhanced by selected antibodies to C1, C4, C5, V3 and anti-CD4 binding site MAbs – enhances binding of selected V3, C4 and anti-CD4 binding site MAbs. Moore & Sodroski [1996]

- G3-4: Described epitope as STSIRGKVKEYAFFYKLDI – binds oligomer – binding of V2 MAbs G3-136, G3-4 or BAT085 did not significantly alter gp120 dissociation from virus or expose the gp41 epitope of MAb 50-69, in contrast to anti-V3 MAbs. Poignard *et al.* [1996a]
- G3-4: Bound preferentially to the monomeric rather than oligomeric form of LAI gp120 – neutralizes Hx10 cell-free virus. Sattentau & Moore [1995]
- G3-4: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V2 loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a – anti-V2 MAbs G3-4 and G3.136 don't bind to T-cell tropic SF2. Stamatatos & Cheng-Mayer [1995]
- G3-4: Reactive with BH10, RF, and MN – binds native, but not denatured or deglycosylated gp120, binds to deglycosylated V1V2 fusion protein, suggesting importance of glycans outside the V1V2 region. Wu *et al.* [1995]
- G3-4: Weakly neutralizing, IC 50 = 53 mug/ml. Gorny *et al.* [1994]
- G3-4: Conformationally sensitive – sporadic cross-reactivity among, and outside, B clade gp120s. Moore *et al.* [1994b]
- G3-4: gp41 mutation (582 A/T) that reduces neutralization of anti-CD4 binding site MAbs does not alter G3-4s ability to neutralize. Thali *et al.* [1994]
- G3-4: Neutralizes RF – substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity and result in neutralization escape. Yoshiyama *et al.* [1994]
- G3-4: Conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120, and does not inhibit HIV-1 sera from binding to IIIB gp120. Moore & Ho [1993]
- G3-4: V2 region, marginal binding to peptide, binding inhibited by 183/184 PI/SG substitution. Moore *et al.* [1993a]
- G3-4: Increased binding in the presence of sCD4. Sattentau *et al.* [1993]
- G3-4: Substitutions in residues 176 to 184 affect MAb recognition – substitutions in V2 can result in gp120-gp41 dissociation. Sullivan *et al.* [1993]
- G3-4: Neutralizes IIIB and RF, not MN – blocks sCD4-gp120, not as potent as MAb 15e – V2 binding MAbs BAT085 and G3-136 block G3-4 gp120 binding – sensitive to reduction of gp120 by DTT. Ho *et al.* [1992]
- G3-4: Binding is sensitive to removal of glycans by endo H – 50% neutralization of 4/9 primary isolates – has conformational features. Ho *et al.* [1991a]

No. 395
MAb ID BAT085 (BAT-085)
HXB2 Location gp160 (171–180)
Author Location gp120 (170–180 IIIB)
Epitope KEYAFFYKLD
Neutralizing L
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
Research Contact Tanox Biosystems Inc and David Ho, ADARC, NY
References Parren *et al.* 1998a; Ditzel *et al.* 1997; Binley *et al.* 1997a; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; Wu *et al.* 1995; Yoshiyama *et al.* 1994; Gorny *et al.* 1994; Moore *et al.* 1994d; D'Souza *et al.* 1994; Moore *et al.* 1993a; Thali *et al.* 1993; Pirofski *et al.* 1993; Moore & Ho 1993; Fung *et al.* 1992; Fung *et al.* 1987

- BAT085: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- BAT085: Binding is blocked by other V2 region antibodies, enhanced by several anti-C1 MAbs, and anti-V3 MAb G511 – reciprocal enhancement of CD4i MAb 48d binding. Moore & Sodroski [1996]
- BAT085: Epitope suggested to be QKEYAFFYKLD – binds oligomer – binding of V2 MAbs G3-136, G3-4 or BAT123 did not significantly alter gp120 dissociation from virus or expose the gp41 epitope of MAb 50-69, in contrast to anti-V3 MAbs. Poignard *et al.* [1996a]
- BAT085: Bound preferentially to the monomeric rather than oligomeric form of LAI gp120 – neutralizes cell free Hx10. Sattentau & Moore [1995]
- BAT085: HXB10 strain specificity – binds native, deglycosylated, or denatured gp120. Wu *et al.* [1995]
- BAT085: Multi-lab study for antibody characterization and assay comparison – did not bind MN or SF2. D'Souza *et al.* [1994]
- BAT085: Interacts with two overlapping peptides with region of overlap KEYAFFYKLD. Gorny *et al.* [1994]
- BAT085: Neutralizes RF – substitution 177 Y/H in the V2 loop of RF does not inhibit neutralization, in contrast to MAbs G3-4 and SC258. Yoshiyama *et al.* [1994]
- BAT085: Called BAT-85 – conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120, and does not inhibit HIV-1 sera from binding to IIIB gp120. Moore & Ho [1993]
- BAT085: 7/8 V2 murine MAbs required gp120 native structure to bind, but BAT085 was the exception – type-specific. Moore *et al.* [1993a]
- BAT085: Peptide affinities of G3-136 and G3-4 are 100-fold less than BAT085, but BAT085 has lower affinity for BH10 gp120 and is weaker at neutralization. Moore *et al.* [1993a]
- BAT085: V2 region – sCD4 does not block – neutralizes IIIB and some primary isolates, but not MN or RF – binds MN – deglycosylation or DDT reduction of gp120 does not diminish reactivity. Fung *et al.* [1992]

No. 396
MAb ID 60b
HXB2 Location gp160 (172–181)
Author Location gp120 (172–181 HXB2)
Epitope EYAFFYKLDI
Subtype B
Neutralizing no
Immunogen Vaccine

Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2b)
References Shotton *et al.* 1995

- 60b: V2 MAb did not neutralize HXB2 – bound to rgp120 in ELISA – substitutions 179-180 LD/DL and 191-193 YSL/GSS abrogate binding, as do changes outside the minimum epitope – competes with 12b, but not 74. Shotton *et al.* [1995]

No. 397
MAb ID 74
HXB2 Location gp160 (172–181)
Author Location gp120 (172–181)
Epitope EYAFFYKLDI
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG1)
References Shotton *et al.* 1995

- 74: V2 MAb did not neutralize HXB2 – did not bind rgp120 ELISA – position 179-180 LD to DL abrogates binding, as do changes outside the minimum epitope – does not compete with 60b or 12b, and is enhanced by two conformation dependent MAbs. Shotton *et al.* [1995]

No. 398
MAb ID 38/12b
HXB2 Location gp160 (172–191)
Author Location gp120 (172–191 HXB2)
Epitope EYAFFYKLDIIPIDNDTTSY
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat
References Wu *et al.* 1995

- 38/12b: Broad specificity: HXB2, MN, SF162 – binds native and deglycosylated gp120. Wu *et al.* [1995]

No. 399
MAb ID 38/60b
HXB2 Location gp160 (172–191)
Author Location gp120 (172–191 HXB2)
Epitope EYAFFYKLDIIPIDNDTTSY
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat
References Wu *et al.* 1995

- 38/60b: Strain specificity: HXB2 – binds native and deglycosylated gp120. Wu *et al.* [1995]

No. 400
MAb ID polyclonal (VEI2)
HXB2 Location gp160 (176–196)
Author Location Env
Epitope FYKLDIVPIDNTTTSYRLISC
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Carlos *et al.* 1999

- Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGP-GRAFYTTGDIGNIRQ. Carlos *et al.* [1999]

No. 401
MAb ID 322-151
HXB2 Location gp160 (211–221)
Author Location gp120 (201–220 LAI)
Epitope EPIPIHYCAPA
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG)
Research Contact G. Robey, Abbot Labs
References Moore *et al.* 1994d; Moore *et al.* 1994c

- 322-151: The relative affinity denatured/native gp120 is 30. Moore *et al.* [1994c]

No. 402
MAb ID 3D3.B8
HXB2 Location gp160 (211–221)
Author Location gp120 (211–220 LAI)
Epitope EPIPIHYCAPA
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG)
References Moore *et al.* 1994c; Bolmstedt *et al.* 1990

- 3D3.B8: The relative affinity denatured/native gp120 is greater than 10. Moore *et al.* [1994c]

No. 403
MAb ID 4C11.D8
HXB2 Location gp160 (211–221)
Author Location gp120 (211–220 LAI)
Epitope EPIPIHYCAPA
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgM)
References Moore *et al.* 1994c; Bolmstedt *et al.* 1990

- 4C11.D8: The relative affinity denatured/native gp120 is greater than 10. Moore *et al.* [1994c]

No. 404
MAb ID 493-156
HXB2 Location gp160 (211–230)

Author Location gp120 (211–230 LAI)
Epitope EPIPIHYCAPAGFAILKCNN
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG)
Research Contact G. Robey, Abbot Labs
References Moore *et al.* 1994c

- 493-156: The relative affinity denatured/native gp120 is >10. Moore *et al.* [1994c]

No. 405
MAb ID 110.1
HXB2 Location gp160 (212–221)
Author Location gp120 (200–217)
Epitope PIPIHYCAPA
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) human
References Valenzuela *et al.* 1998; Pincus *et al.* 1996; Pincus & McClure 1993

- 110.1: There is another antibody with this ID that binds to Env at positions 491-500 in LAI, see.
- 110.1: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding – 110.1-RAC did not mediate cell killing, and sCD4 has no effect. Pincus & McClure [1993]; Pincus *et al.* [1996]

No. 406
MAb ID GV4H3
HXB2 Location gp160 (219–226)
Author Location gp120 (219–226 IIIB)
Epitope APAGFAIL
Neutralizing
Immunogen Vaccine
Vector/Type: protein-Ab complex *HIV component:* gp120-Mab complex
Species (Isotype) mouse
References Denisova *et al.* 1996

- GV4H3: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes. Denisova *et al.* [1996]

No. 407
MAb ID J1
HXB2 Location gp160 (222–231)
Author Location gp120 (222–231 LAI)
Epitope GFAILKCNNK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI
Species (Isotype) mouse (IgG1)
Research Contact J. Hoxie, U. Penn.
References Cook *et al.* 1994; Moore *et al.* 1994d; Moore *et al.* 1994c

- J1: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. Cook *et al.* [1994]
- J1: The relative affinity denatured/native gp120 is 30. Moore *et al.* [1994c]

No. 408
MAb ID J3
HXB2 Location gp160 (222–231)
Author Location gp120 (222–231 LAI)
Epitope GFAILKCNNK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI
Species (Isotype) mouse (IgG1)
Research Contact J. Hoxie, U. Penn.
References Cook *et al.* 1994; Moore *et al.* 1994c

- J3: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. Cook *et al.* [1994]
- J3: The relative affinity denatured/native gp120 is 30. Moore *et al.* [1994c]

No. 409
MAb ID 1006-30-D
HXB2 Location gp160 (236–245)
Author Location gp120 (241–251)
Epitope KGSCKNVSTV
Neutralizing
Immunogen
Species (Isotype) human (IgG1λ)
Ab Type C2
References Nyambi *et al.* 2000; Hioe *et al.* 2000

- 1006-30-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C2 MAbs 1006-30-D and 847-D did not effect proliferation. Hioe *et al.* [2000]
- 847-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including two C2 MAbs – the binding of anti-C2 MAbs was weak to isolates from clades B, C, D, E, F, G, and they did not not bind to isolates from subtypes A and H – epitope is suggested to be in a 20 amino acid peptide KGSCKNVSTVQCTHGIRPVV. Nyambi *et al.* [2000]

No. 410
MAb ID 847-D
HXB2 Location gp160 (236–245)
Author Location gp120 (241–251)
Epitope KGSCKNVSTV
Neutralizing
Immunogen
Species (Isotype) human (IgG1λ)
Ab Type C2

References Nyambi *et al.* 2000; Hioe *et al.* 2000

- 847-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C2 MAbs 1006-30-D and 847-D did not effect proliferation. Hioe *et al.* [2000]
- 847-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including two C2 MAbs – the binding of anti-C2 MAbs was weak to isolates from clades B, C, D, E, F, G, and they did not not bind to isolates from subtypes A and H – epitope is suggested to be in a 20 amino acid peptide KGSCKNVSTVQCTHGIRPVV. Nyambi *et al.* [2000]

No. 411
MAb ID MF169.1
HXB2 Location gp160 (252–261)
Author Location gp120 (242–261 LAI)
Epitope RPVVSTQLLL
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
References Moore *et al.* 1994d; Moore *et al.* 1994c; Thiriart *et al.* 1989

- MF169.1: The relative affinity denatured/native gp120 is 11 – mutations 252 R/W, 257 T/G, and 257 T/R impair binding. Moore *et al.* [1994c]

No. 412
MAb ID MF170.1
HXB2 Location gp160 (252–261)
Author Location gp120 (242–261 LAI)
Epitope RPVVSTQLLL
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
References Moore *et al.* 1994d; Moore *et al.* 1994c; Thiriart *et al.* 1989

- MF170.1: The relative affinity denatured/native gp120 is 15 – mutations 252 R/W, 257 T/G, and 257 T/R impair binding to denatured and native gp120, and 262N/T, 269 E/L and 281 A/V to only native gp120. Moore *et al.* [1994c]

No. 413
MAb ID MF87.1
HXB2 Location gp160 (252–261)
Author Location gp120 (242–261 LAI)
Epitope RPVVSTQLLL
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- MF87.1: The relative affinity denatured/native gp120 is 10 – mutations 252 R/W, 257 T/G, and 257 T/R impair binding. Moore *et al.* [1994c]

No. 414
MAb ID 213.1
HXB2 Location gp160 (252–261)
Author Location gp120 (242–261 LAI)
Epitope RPVVSTQLLL
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG1)
Ab Type C2
Research Contact Claudine Bruck
References Moore *et al.* 1994c; Moore & Ho 1993; Thiriart *et al.* 1989

- 213.1: UK Medical Research Council AIDS reagent: ARP334.
- 213.1: The relative affinity denatured/native gp120 is 100 – mutations 252 R/W, 257 T/G or T/R impair binding. Moore *et al.* [1994c]
- 213.1: Bound preferentially to denatured IIIB and SF2 gp120. Moore & Ho [1993]

No. 415
MAb ID B12
HXB2 Location gp160 (252–271)
Author Location gp120 (252–271 LAI)
Epitope RPVVSTQLLLNGSLAEEEVV
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG)
Ab Type C2
References Maksiutov *et al.* 2002; Moore *et al.* 1994c

- B12: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. Maksiutov *et al.* [2002]
- B12: C2 region – the relative affinity for denatured/native gp120 is 27 – mutations 257 T/R and 262 N/T impair binding. Moore *et al.* [1994c]

No. 416
MAb ID B13 (Bh13, Chessie B13)
HXB2 Location gp160 (252–271)
Author Location gp120 (252–271 LAI)
Epitope RPVVSTQLLLNGSLAEEEVV
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG2a)
Ab Type C2
Research Contact George Lewis, Institute of Human Virology, Baltimore MD, USA

References Maksiutov *et al.* 2002; Wang *et al.* 2002c; Connor *et al.* 1998; Pincus *et al.* 1996; Moore *et al.* 1994d; Abacioglu *et al.* 1994; Moore *et al.* 1994c; Moore & Ho 1993; Pincus & McClure 1993

- B13: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. Maksiutov *et al.* [2002]
- B13: Called Bh13 – binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect. Pincus & McClure [1993]; Pincus *et al.* [1996]
- B13: C2 region – epitope boundaries mapped by peptide scanning, core epitope: TQLLLN. Abacioglu *et al.* [1994]
- B13: The relative affinity for denatured/native gp120 is 30 – mutations 257 T/R and 269 E/L impair binding. Moore *et al.* [1994c]
- B13: Bound preferentially to denatured IIIB gp120. Moore & Ho [1993]

No. 417
MAb ID C13
HXB2 Location gp160 (252–271)
Author Location gp120 (252–271 LAI)
Epitope RPVVSTQLLLNGSLAEEEVV
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG1)
Ab Type C2
Research Contact George Lewis
References Maksiutov *et al.* 2002; Abacioglu *et al.* 1994; Moore *et al.* 1994c; Moore & Ho 1993

- C13: NIH AIDS Research and Reference Reagent Program: 1209.
- C13: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. Maksiutov *et al.* [2002]
- C13: Epitope boundary extended to RPVVSTQLLL-NGSLAEEEVVIR, to take into account the effect of a point mutation. Abacioglu *et al.* [1994]
- C13: The relative affinity for denatured/native gp120 is 36 – mutations 257 T/R, 267 E/L, and 269 E/L impair binding. Moore *et al.* [1994c]
- C13: Bound preferentially to denatured IIIB gp120. Moore & Ho [1993]

No. 418
MAb ID M89
HXB2 Location gp160 (252–271)
Author Location gp120 (252–271 LAI)
Epitope RPVVSTQLLLNGSLAEEEVV
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse (IgG1)
Ab Type C2
Research Contact Fulvia di Marzo Veronese
References Maksiutov *et al.* 2002; Moore *et al.* 1994d; Moore *et al.* 1994c; di Marzo Veronese *et al.* 1992

- M89: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. Maksiutov *et al.* [2002]
- M89: C2 region – the relative affinity for denatured/native gp120 is >30 – mutations 257 T/R and 269 E/L impair binding. Moore *et al.* [1994c]
- M89: Immunoblot reactive, RIP negative, for strains IIIB, 451, MN, RF, and RUTZ. di Marzo Veronese *et al.* [1992]

No. 419
MAb ID B21
HXB2 Location gp160 (257–262)
Author Location gp120 (257–262 BH10)
Epitope TQLLLN
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG1)
Ab Type C2
References Abacioglu *et al.* 1994

- B21: C2 region, epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 420
MAb ID B23
HXB2 Location gp160 (257–262)
Author Location gp120 (257–262 BH10)
Epitope TQLLLN
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG2a)
Ab Type C2
References Abacioglu *et al.* 1994

- B23: C2 region, epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 421
MAb ID B24
HXB2 Location gp160 (257–262)
Author Location gp120 (257–262 BH10)
Epitope TQLLLN
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) mouse (IgG2a)
Ab Type C2
References Abacioglu *et al.* 1994

- B24: C2 region, epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 422
MAb ID B25

HXB2 Location gp160 (257–262)
Author Location gp120 (257–262 BH10)
Epitope TQLLLN
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
Ab Type C2
References Abacioglu *et al.* 1994

- B25: C2 region, epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 423
MAb ID B3
HXB2 Location gp160 (257–262)
Author Location gp120 (257–262 BH10)
Epitope TQLLLN
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
Ab Type C2
References Abacioglu *et al.* 1994

- B3: C2 region, epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 424
MAb ID B26
HXB2 Location gp160 (257–263)
Author Location gp120 (257–263 BH10)
Epitope TQLLLNG
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
Ab Type C2
References Abacioglu *et al.* 1994

- B26: C2 region, epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 425
MAb ID B29
HXB2 Location gp160 (257–263)
Author Location gp120 (257–263 BH10)
Epitope TQLLLNG
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG2a)
Ab Type C2
References Abacioglu *et al.* 1994

- B29: C2 region, epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 426
MAb ID B36
HXB2 Location gp160 (257–263)
Author Location gp120 (257–263 BH10)
Epitope TQLLLNG
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
Ab Type C2
References Abacioglu *et al.* 1994

- B36: C2 region, epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 427
MAb ID 110.E
HXB2 Location gp160 (262–281)
Author Location gp120 (262–281 LAI)
Epitope NGSLAEEEVVIRSVNFTDNA
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: Env
Species (Isotype) mouse (IgG)
Ab Type C2
Research Contact F. Traincard
References Maksiutov *et al.* 2002; Moore *et al.* 1994d; Moore *et al.* 1994c

- 110.E: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. Maksiutov *et al.* [2002]
- 110.E: The relative affinity for denatured/native gp120 is 7.3. Moore *et al.* [1994c]

No. 428
MAb ID 110.C
HXB2 Location gp160 (271–280)
Author Location gp120 (271–280 LAI)
Epitope VIRSVNFTDN
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: Env
Species (Isotype) mouse (IgG)
Ab Type C2
Research Contact F. Traincard, Hybridolabs, Institut Pasteur
References Valenzuela *et al.* 1998; Moore *et al.* 1994d; Moore *et al.* 1994c

- 110.C: Only slightly reduces LAI viral binding or entry into CEM cells. Valenzuela *et al.* [1998]
- 110.C: The relative affinity for denatured/native gp120 is 1. Moore *et al.* [1994c]

No. 429
MAb ID IIIB-V3-26
HXB2 Location gp160 (291–307)
Author Location gp120 (299–304 IIIB)
Epitope SVEINCTRPNNNTRKSI
Neutralizing no

Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (Isotype) mouse (IgG1)
Ab Type V3
References Maksiutov *et al.* 2002; Laman *et al.* 1992

- IIIB-V3-26: This epitope is similar to a fragment of the FasI receptor precursor (Apptosis-mediating surface antigen fas) (APO- 1 antigen) (CD95 antigen), VEINCTRQN. Maksiutov *et al.* [2002]
- IIIB-V3-26: Binds to the base of the V3 loop on denatured gp120. Laman *et al.* [1992]

No. 430
MAb ID IIIB-V3-21 (V3-21)
HXB2 Location gp160 (294–299)
Author Location gp120 (299–304 IIIB)
Epitope INCTRP
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (Isotype) mouse (IgG1)
Ab Type V3
Research Contact J. Laman
References Ling *et al.* 2004; Maksiutov *et al.* 2002; Zhang *et al.* 2002; Valenzuela *et al.* 1998; Laman *et al.* 1993; Laman *et al.* 1992
Keywords antibody binding site definition and exposure

- IIIB-V3-21: UK Medical Research Council AIDS reagent: ARP3048.
- IIIB-V3-21: NIH AIDS Research and Reference Reagent Program: 1725.
- IIIB-V3-21: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of the V3 MAbs 694-98D and 447-52D, that both bind near the tip of the loop, was decreased by both thrombin and trypsin, but anti-V3 MAb IIIB-V3-21 was not decreased in either case. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- IIIB-V3-21: This epitope is similar to a fragment of the FasI receptor precursor (Apptosis-mediating surface antigen fas) (APO- 1 antigen) (CD95 antigen), VEINCTRQN. Maksiutov *et al.* [2002]
- IIIB-V3-21: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002]
- IIIB-V3-21: Does not block HIV-1 LAI binding or entry into CEM cells. Valenzuela *et al.* [1998]
- IIIB-V3-21: Binds to NP40 treated gp120, and epitope is probably obscured by local glycosylation. Laman *et al.* [1993]
- IIIB-V3-21: Binds to the base of the V3 loop on denatured gp120. Laman *et al.* [1992]

No. 431
MAb ID 168B8
HXB2 Location gp160 (296–317)
Author Location gp120 (BaL)
Epitope CTRPNYNKRKHIGPGRAF
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: gp120-CD4 complex *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) humanized mouse (IgG2κ)
Ab Type V3
Research Contact Abraham Pinter, Lab. of Retrovirology, Public Research Institute, pinter@phri.org
References He *et al.* 2003
Keywords antibody binding site definition and exposure, vaccine antigen design

- 168B8: Vaccination of a gp120-CD4 fusion complex in six transgenic XMG2 XenoMouse mice that produce human IgG2 with K light chain did not produce any neutralizing antibodies. 36/39 MAbs derived from one of these mice were in one of two competition groups that were conformational and specific for the complex, suggesting this chimeric vaccine may be of little value, as immunodominant responses are to epitopes unique to the complex, not present in native Env. This MAb is one of the 3/36 non-neutralizing MAbs that bound to linear epitopes on gp120. He *et al.* [2003] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 432
MAb ID polyclonal
HXB2 Location gp160 (296–331)
Author Location gp120 (MN)
Epitope CNYNKRKRIHIGPGRAFYTTKNIIGTIC
Neutralizing L
Immunogen
Species (Isotype) rabbit (IgA, IgG)
Ab Type V3
References FitzGerald *et al.* 1998

- Polyclonal response to MN, or Thai E V3 loop inserted into Pseudomonas Exotoxin for vaccination – inserts of 14 or 26 amino acids were used from MN or a Thai E strain, constrained by disulfide bond – sera from vaccinated rabbit were reactive with strain-specific gp120 – administration to mucosal surfaces elicits IgA. FitzGerald *et al.* [1998]

No. 433
MAb ID polyclonal
HXB2 Location gp160 (297–330)
Author Location Env (303–335 LAI)
Epitope TRPNNNTRKSIHIGPGRAFYATGEIIGDIRQAH
Subtype B
Neutralizing no
Immunogen Vaccine

Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* V3 *Adjuvant:* QS21
Species (Isotype) human (IgG)
Ab Type V3
References Pialoux *et al.* 2001

- 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28 (89%), proliferative in 19/28 (79%), and CTL in 13/24 (54%) of testable volunteers – 14/28 had non-neutralizing Ab responses to this peptide (E), 7/24 had proliferative responses, and multiple CTL responses were detected. Pialoux *et al.* [2001]

No. 434
MAb ID MO97/V3
HXB2 Location gp160 (299–308)
Author Location gp120 (299–308 IIIB)
Epitope PNNNTRKSIR
Neutralizing no
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
Ab Type V3
References Gorny & Zolla-Pazner 2004; Ohlin *et al.* 1992
Keywords review

- M097/V3: Review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains; a subset can also neutralize some primary isolates. The three IgMs, M096, M097, and M099, are non-neutralizing. Gorny & Zolla-Pazner [2004] (**review**)
- MO97: Generated through *in vitro* stimulation of uninfected-donor lymphocytes with rpB1 (IIIB Env 286-467) Ohlin *et al.* [1992]

No. 435
MAb ID polyclonal
HXB2 Location gp160 (299–331)
Author Location gp120 (306–338 BH10)
Epitope PNNNTRKSIRIQRGPGRAFVTIGKIGNMRQAHC
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10
Species (Isotype) rabbit (IgG)
Ab Type V3
References Neurath & Strick 1990

- 21 V3 loop variant peptides spanning this region were tested and serological cross-reactivity correlated with divergence. Neurath & Strick [1990]

No. 436
MAb ID 55/1l
HXB2 Location gp160 (300–315)
Author Location gp120 (300–315)
Epitope NNNTRKRIRIQRGPGR?
Neutralizing
Immunogen
Species (Isotype)
Ab Type V3
References Peet *et al.* 1998

- 55/1l: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/1l binding was abrogated by V3 serine substitutions in the V3 loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]

No. 437
MAb ID 8/38c (8/38/1c)
HXB2 Location gp160 (300–315)
Author Location gp120 (300–315 HXB10)
Epitope NNNTRKRIRIQRGPGR
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2a)
Ab Type V3
Research Contact C. Dean and C. Shotton, Institute for Cancer Research, Surrey, UK
References Peet *et al.* 1998; Parren *et al.* 1998a; Jeffs *et al.* 1996; Sattentau & Moore 1995; McKeating *et al.* 1992a

- 8/38c: UK Medical Research Council AIDS reagent: ARP3039.
- 8/38c: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- 8/38c: Called 8/38/1c: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 8/38c binding was only diminished by V3 serine substitutions C-term to the tip of the loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]
- 8/38c: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120. Jeffs *et al.* [1996]
- 8/38c: Binds equally well to monomer and oligomer, less rapid association rate than other anti-V3 antibodies, and an associated less potent neutralization of lab strains. Sattentau & Moore [1995]
- 8/38c: Binds to virion gp120 and neutralizes only in the presence of sCD4. McKeating *et al.* [1992a]

No. 438
MAb ID 8/64b
HXB2 Location gp160 (300–315)
Author Location gp120 (300–315 HXB10)
Epitope NNNTRKRIRIQRGPGR
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120

Species (Isotype) rat (IgM)
Ab Type V3
References Peet *et al.* 1998; McKeating *et al.* 1992a

- 8/64b: UK Medical Research Council AIDS reagent: ARP3036.
- 8/64b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 8/64b binding was abrogated by V3 serine substitutions C-term to the tip of the loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]
- 8/64b: Binds to virion gp120 and neutralizes only in the presence of sCD4. McKeating *et al.* [1992a]

No. 439
MAb ID polyclonal
HXB2 Location gp160 (300–321)
Author Location gp120
Epitope NYNKRKRIHIGPGRAFYTTK
Neutralizing L
Immunogen HIV-1 infection, Vaccine
Vector/Type: peptide *HIV component:* V3
Species (Isotype) human
Ab Type V3
References Bartlett *et al.* 1998

- V3 peptide vaccine (MN, RF, EV91, and Can0A) with a C4 helper T cell epitope were used to vaccinate HLA-B7 HIV-infected patients – V3 Ab levels and the anti-HIV proliferative response, but no decrease in HIV-1 RNA levels or increase in CD4 levels was observed. Bartlett *et al.* [1998]

No. 440
MAb ID polyclonal
HXB2 Location gp160 (300–321)
Author Location gp120
Epitope NYNKRKRIHIGPGRAFYTTK
Neutralizing
Immunogen HIV-1 exposed seronegative
Species (Isotype) human (IgA)
Ab Type V3
References Kaul *et al.* 1999

- HIV-1 Env-specific mucosal IgA found in genital track of 16/21 HIV-1 resistant chronically exposed Kenyan sex workers – 11/21 had detectable Th responses. Kaul *et al.* [1999]

No. 441
MAb ID polyclonal
HXB2 Location gp160 (300–322)
Author Location gp120 (IIIB)
Epitope CNNTRKSIRIQRGPGRAFVTIGK
Neutralizing L
Immunogen
Species (Isotype) guinea pig (IgG)
Ab Type V3
Research Contact D. Bolognesi and T. Matthews, Duke University
References Allaway *et al.* 1993

- Synergy with combinations of CD4-based molecules in inhibition of HIV-1 Env mediated cell fusion. Allaway *et al.* [1993]

No. 442
MAb ID polyclonal (VEI3)
HXB2 Location gp160 (300–328)
Author Location Env
Epitope NNNTRKSIRIGPGRAFYTTGDIGNIRQ
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
References Carlos *et al.* 1999

- Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGP-GRAFYTTGDIGNIRQ. Carlos *et al.* [1999]

No. 443
MAb ID 9284 (NEA 9284)
HXB2 Location gp160 (301–312)
Author Location gp120 (307–318 IIIB)
Epitope NNTRKSIRIQRG
Neutralizing L
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
Ab Type V3
Research Contact Dupont de Nemours, Les Ulis, France or Wilmington, Delaware
References Schonning *et al.* 1998; Parren *et al.* 1998a; Binley *et al.* 1997a; Cao *et al.* 1997b; Poignard *et al.* 1996a; Moore & Sodroski 1996; Fontenot *et al.* 1995; VanCott *et al.* 1995; Sattentau & Moore 1995; Sorensen *et al.* 1994; Okada *et al.* 1994; Cook *et al.* 1994; Thali *et al.* 1994; VanCott *et al.* 1994; Thali *et al.* 1993; Trujillo *et al.* 1993; Moore *et al.* 1993b; Sattentau *et al.* 1993; McKeating *et al.* 1992a; Wyatt *et al.* 1992; Sattentau & Moore 1991; Skinner *et al.* 1988a; Skinner *et al.* 1988b

- 9284: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- 9284: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, 9284 was found to have an inaccessible epitope on the oligomeric form of Env and anti-V3 MAbs were found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan more efficiently than HIV-BRU. Schonning *et al.* [1998]

- 9284: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4. Cao *et al.* [1997b]
- 9284: Binds V3 loop – anti-C1 MAbs 133/290 and 135/9 enhance binding – reciprocal binding inhibition of other anti-V3 MAbs. Moore & Sodroski [1996]
- 9284: V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus, mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs. Poignard *et al.* [1996a]
- 9284: Binds equally well to monomer and oligomer, rapid association and potent neutralization of lab strains – neutralizes cell-free virus Hx10. Sattentau & Moore [1995]
- 9284: Used to monitor HIV-1 Env expression in infected H9 cells, binds native and reduced gp120s similarly. VanCott *et al.* [1995]
- 9284: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro*. Cook *et al.* [1994]
- 9284: Binding domain aa 301-310: TRKSIRIQRG – mutations in the V3 loop from basic residues can destroy virus infectivity and syncytium formation: R306T, R309T and R313G can also reduce binding of V3 MAbs with two different binding sites: 9284 and 0.5beta – called NEA9284. Okada *et al.* [1994]
- 9284: Did not neutralize infection of HIV/HTLV-I pseudotype. Sorensen *et al.* [1994]
- 9284: gp41 mutation that confers resistance to neutralization by anti-CD4 binding site antibodies does not reduce neutralizing efficiency of this V3 region MAb. Thali *et al.* [1994]
- 9284: Does not bind MN gp120, just IIIB. VanCott *et al.* [1994]
- 9284: Inhibits C4 region antibodies (G3-299, G3-519) which have conformational requirements. Moore *et al.* [1993b]
- 9284: Increased binding in the presence of sCD4. Sattentau *et al.* [1993]
- 9284: Peptide RIQRGPGRAFVTIGKIGNMRQA – Reacts with three human brain proteins of 35, 55, 110 kd – called NEA-9284. Trujillo *et al.* [1993]
- 9284: Single amino acid substitutions in the C4 region (427 W/V or W/S) or at the base of the V3 loop (298 R/G) can significantly increase binding and neutralization– position 427 is also important for CD4 binding and anti-CD4 binding site MAbs. Wyatt *et al.* [1992]
- 9284: Two fold increase in binding to gp120 in the presence of bound sCD4. Sattentau & Moore [1991]
- 9284: IIIB type-specific binding and neutralization. Skinner *et al.* [1988b]

No. 444
MAb ID polyclonal
HXB2 Location gp160 (301–325)
Author Location gp120 (IIIB)
Epitope NNTRKSIRIQRGPGRAFVTIGKIGN
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *Adjuvant:* Cholera toxin (CT)
Species (Isotype) mouse (IgA)
Ab Type V3
References Bukawa *et al.* 1995

- Polyclonal secretory IgA antibody raised by mucosal immunization is able to neutralize IIIB, SF2, and MN – HIV-1 neutralization may be due to V3, CD4 or HPG30 component of the multicomponent peptide immunogen. Bukawa *et al.* [1995]

No. 445
MAb ID polyclonal
HXB2 Location gp160 (301–325)
Author Location gp120 (IIIB)
Epitope NNTRKSIRIQRGPGRAFVTIGKIGN
Neutralizing L
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* Env, Rev
Species (Isotype) mouse (IgA22a)
Ab Type V3
References Sasaki *et al.* 1998

- An anti-env response was sought, and co-expression of Rev was required – intramuscular versus nasal vaccination with DNA vaccine with a QS21 adjuvant was studied – QS21 enhanced the IgG2a response mediated via Th1 cytokines IFNgamma and IL-2. Sasaki *et al.* [1998]

No. 446
MAb ID polyclonal
HXB2 Location gp160 (302–317)
Author Location Env (B consensus)
Epitope NTRKSIHIGPGRAF
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
References Morris *et al.* 2001

- Ab responses before HAART therapy and after one year of therapy were measured in 8 individuals that were classified HAART successes, and 10 patients who were classified as HAART failures – V3 peptide antibody binding titers to the B-consensus and MN and SF2 variants, and neutralization of HIV-1 MN and four subtype B clinical isolates were tested – subjects with strong anti-V3 and NAb humoral immune responses before starting HAART were more likely to achieve sustained viral suppression to <500 copies RNA/ml on HAART – HIV-specific Ab responses declined after 1 year of successful viral suppression on HAART. Morris *et al.* [2001]

No. 447
MAb ID polyclonal
HXB2 Location gp160 (302–318)
Author Location Env
Epitope NTRKSIHIGPGRAFY
Neutralizing L P
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
References Bongertz *et al.* 2001

- Non-transmitting mothers had an increased frequency of high neutralizing plasma Ab titers against HIV-1 MN (1:50 dilution, >90% neutralization, 33/88 pregnant women), compared to plasma from transmitting mothers (0/8 pregnant women) – non-transmitting mothers also had more potent neutralization against primary isolates from transmitting mothers, but neutralization of autologous virus was comparable for non-transmitting (7/13) and transmitting mothers (2/4) Bongertz *et al.* [2001]

No. 448
MAb ID MAG 109
HXB2 Location gp160 (302–321)
Author Location gp120 (302–321 BH10)
Epitope NTRKSIRIQRGPGRAFVTIG
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type V3
References Kang *et al.* 1994

- MAG 109: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) Kang *et al.* [1994]

No. 449
MAb ID MAG 49 (#49)
HXB2 Location gp160 (302–321)
Author Location gp120 (302–321 BH10)
Epitope NTRKSIRIQRGPGRAFVTIG
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type V3
References Moore & Sodroski 1996; Kang *et al.* 1994

- MAG 49: Called #49 in this text. Binding enhanced by anti-C1 MAbs 133/290, 135/9, and by many anti-CD4 binding site MAbs – reciprocal enhancement of some anti-V2 MAbs – reciprocal binding inhibition of anti-V3 MAbs. Moore & Sodroski [1996]
- MAG 49: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) Kang *et al.* [1994]

No. 450
MAb ID MAG 53
HXB2 Location gp160 (302–321)
Author Location gp120 (302–321 BH10)
Epitope NTRKSIRIQRGPGRAFVTIG
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type V3
References Kang *et al.* 1994

- MAG 53: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) Kang *et al.* [1994]

No. 451
MAb ID MAG 56
HXB2 Location gp160 (302–321)
Author Location gp120 (302–321)
Epitope NTRKSIRIQRGPGRAFVTIG
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type V3
References Kang *et al.* 1994

- MAG 56: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) Kang *et al.* [1994]

No. 452
MAb ID 1324-E (1324E)
HXB2 Location gp160 (303–308)
Author Location Env (subtype CRF01)
Epitope TRTSVR
Subtype CRF01_AE
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Gorny *et al.* 1998
Keywords antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 1324-E: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 1324-E: Called 1324E – A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1324E showed poor cross-reactivity, and was the only MAb tested that was derived from a non-B clade infected patient, an E clade infection was the source of 1324E. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 1324-E: E clade stimulated MAb did not cross-react with B clade peptides nor did B clade derived peptides with an E clade V3 loop, but both E and B clade stimulated Abs can cross-react with some peptides from other clades – this Ab showed strong binding to several E, A and F peptides, one C peptide, and no reactivity with B peptides and most D peptides. Zolla-Pazner *et al.* [1999a] (**inter-clade comparisons**)

- 1324-E: MAb reacted with peptides from E clade, while B clade derived MAbs could not. Zolla-Pazner *et al.* [1999b] (**inter-clade comparisons**)
- 1324-E: A human MAb was derived from an HIV-1 E clade infection from a US service man who had served in Thailand, selected with the consensus V3 peptide from clade E – cross-reactive with V3 peptides, and gp120 from E, C and A clades, as well as cells infected with a C-clade primary isolate, but not with B and D clade V3 peptides or rgp120 – neutralizes E clade virus adapted for growth in H9 cells, but not 5 primary E clade isolates, including the autologous isolate – kinetic parameters were measured, 1324E was comparable to 447-52D. Gorny *et al.* [1998] (**antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 453
MAb ID polyclonal
HXB2 Location gp160 (303–319)
Author Location gp120 (subtype C)
Epitope CKRKIHIGPGQAFYT
Subtype C
Neutralizing
Immunogen Vaccine
Vector/Type: peptide in ISCOM, peptide in liposome *HIV component:* V3 *Adjuvant:* Immune stimulating complexes (ISCOM)
Species (Isotype) mouse (IgG2a, IgG2b)
Ab Type V3
References Ahluwalia *et al.* 1997

- A V3 loop peptide modified to resemble an Indian form (GPGQ) was incorporated into ISCOMS (immune stimulating complexes) or liposomes, and used to immunize mice – the IgG2a/IgG2b antibody response was enhanced by the presentation in the ISCOM suggestive of a Th1 response. Ahluwalia *et al.* [1997]

No. 454
MAb ID MO99/V3
HXB2 Location gp160 (304–308)
Author Location gp120 (304–308 IIIB)
Epitope RKSIR
Neutralizing no
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
Ab Type V3
References Gorny & Zolla-Pazner 2004; Ohlin *et al.* 1992
Keywords antibody binding site definition and exposure, antibody generation

- M099/V3: Review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains; a subset can also neutralize some primary isolates. The three IgMs, M096, M097, and M099, are non-neutralizing. Gorny & Zolla-Pazner [2004]
- MO99: Generated through *in vitro* stimulation of uninfected-donor lymphocytes with rpB1 (IIIB Env 286-467) Ohlin *et al.* [1992] (**antibody binding site definition and exposure**, **antibody generation**)

No. 455
MAb ID C311E
HXB2 Location gp160 (304–313)
Author Location gp120 (309–316 MN)
Epitope RKRIHIGP
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) chimpanzee (IgG1)
Ab Type V3
References Alsmadi & Tilley 1998; Warrier *et al.* 1996

- C311E: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – C311E bound and directed lysis against all four strains. Alsmadi & Tilley [1998]
- C311E: Chimps were infected with HIV-1 IIIB, and this resulting MAb gave synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. Warrier *et al.* [1996]

No. 456
MAb ID 907
HXB2 Location gp160 (304–314)
Author Location gp120 (309–318)
Epitope RKSIRIQRGPG
Neutralizing L
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (Isotype) mouse (IgG1κ)
References Pincus *et al.* 1996; Pincus *et al.* 1991; Pincus *et al.* 1989; Chesebro & Wehrly 1988

- 907: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. Pincus *et al.* [1996]
- 907: Epitope sequence is based on database count of a specified location – 924-RAC immunotoxin is IIIB strain-specific. Pincus *et al.* [1991]
- 907: Coupled to ricin A chain (RAC), MAb 907 inhibited protein synthesis and cell growth in HIV-infected cells. Pincus *et al.* [1989]
- 907: Strain specific binding, and neutralization of only the LAV strain. Chesebro & Wehrly [1988]

No. 457
MAb ID 924
HXB2 Location gp160 (304–314)
Author Location gp120 (309–318 IIIB)
Epitope RKSIRIQRGPG
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp160
Species (Isotype) mouse (IgG1κ)
Ab Type V3
References Pincus *et al.* 1998; Pincus *et al.* 1996; Cook *et al.* 1994; Pincus *et al.* 1993; Pincus & McClure 1993; Pincus *et al.* 1991; Chesebro & Wehrly 1988

- 924: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. Pincus *et al.* [1996]
- 924: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro*. Cook *et al.* [1994]
- 924: MAb was coupled to ricin A chain (RAC) – immunotoxin efficacy was not significantly decreased by sCD4, although the efficacy of gp41 MAb immunotoxins *in vitro* increased 30-fold by sCD4. Pincus & McClure [1993]
- 924: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – MAb 924 was used as a control – infected lab workers and a vaccinia gp160 vaccine had strong V3 MAb response, but alum absorbed rec gp160 did not generate anti-V3 response. Pincus *et al.* [1993]
- 924: Epitope sequence is based on database count of a specified location – 924-RAC immunotoxin is IIIB strain-specific. Pincus *et al.* [1991]
- 924: HIV IIIB strain specific. Chesebro & Wehrly [1988]

No. 458
MAb ID polyclonal
HXB2 Location gp160 (304–318)
Author Location gp120 (304–318 LAI)
Epitope RKSIRIQRGPGRAFV
Subtype B
Neutralizing
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgG, IgM)
Ab Type V3
References Chin *et al.* 1995

- Mimicking the humoral immune response *in vitro* supports isotype switching – human IgG MAbs were generated from naive donors. Chin *et al.* [1995]

No. 459
MAb ID polyclonal
HXB2 Location gp160 (304–318)
Author Location gp120 (304–318 LAI)
Epitope RKSIRIQRGPGRAFV
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI
Species (Isotype) human (IgG, IgM)
Ab Type V3
References Zafiropoulos *et al.* 1997

- IgG to IgM isotype switching in response to primary and secondary peptide vaccinations was studied – the immunogen contained a V3 loop fragment and a tetanus toxin helper epitope. Zafiropoulos *et al.* [1997]

No. 460
MAb ID polyclonal
HXB2 Location gp160 (304–318)
Author Location gp120 (NY5)
Epitope KKGIAIGPGRTLY
Neutralizing
Immunogen
Species (Isotype) (IgM)
Ab Type V3
References Metlas *et al.* 1999a; Metlas *et al.* 1999b

- Auto-Abs that react with the V3 loop of NY5 are present in the sera of HIV- individuals, and are predominantly IgM. Metlas *et al.* [1999b]

No. 461
MAb ID 10F10
HXB2 Location gp160 (304–320)
Author Location gp120 (MN)
Epitope RKRIHIGPGRAFYTT
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN
HIV component: gp120
Species (Isotype) mouse (IgG1)
Ab Type V3
References Duarte *et al.* 1994

- 2C4: Putative epitope lies within IHIGPGRAFYT – generated by multi-epitope polypeptide immunization – recognize MN and SC (TRSIHIGPGRAFYTT) peptides, lower affinity for SF2. Duarte *et al.* [1994]

No. 462
MAb ID 2C4
HXB2 Location gp160 (304–320)
Author Location gp120 (MN)
Epitope RKRIHIGPGRAFYTT
Neutralizing L (MN)
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN
Species (Isotype) mouse (IgG2a)
Ab Type V3
References Duarte *et al.* 1994

- 2C4: Putative epitope lies within IHIGPGRAFYT – neutralizes MN, not IIIB and SF2 – generated by multi-epitope polypeptide immunization – recognize MN and SC (TRSIHIGPGRAFYTT) peptides, lower affinity for SF2. Duarte *et al.* [1994]

No. 463
MAb ID 412-D (412-10D, 412, 412D)
HXB2 Location gp160 (304–320)
Author Location gp120 (MN)
Epitope RKRIHIGPGRAFYTT
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Nyambi *et al.* 1998; Gorny *et al.* 1998; Fontenot *et al.* 1995; VanCott *et al.* 1994; Spear *et al.* 1993; Gorny *et al.* 1993

Keywords antibody binding site definition and exposure, binding affinity, complement, inter-clade comparisons, kinetics, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- 412-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 412-D: Called 412: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 412-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 412-D showed limited reactivity. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 412-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 412-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 391.5, 412 and 418, all selected with MN V3 peptide – the core amino acids HIGPGR tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 412-D: Kinetic parameters were measured, and the association rates were similar, but dissociation rate constants were quite variable for V3 MAbs, 412-D has a relatively fast dissociation, thus low affinity among V3 MAbs. Gorny *et al.* [1998] (**kinetics**)
- 412-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 412-D was bound only to B clade virions and to D clade MAL. Nyambi *et al.* [1998] (**inter-clade comparisons**)
- 412-D: Called 412 – The tip of the V3 loop was presented in a mucin backbone – higher valency correlates with higher affinity constant. Fontenot *et al.* [1995] (**vaccine antigen design**, **binding affinity**)
- 412-D: Called 412-10D – relatively rapid dissociation and weak homologous neutralization. VanCott *et al.* [1994] (**binding affinity**)
- 412-D: Neutralizes MN, does not bind SF2 or HXB2 – not reactive with hexa or heptapeptides by Pepscan. Gorny *et al.* [1993] (**variant cross-recognition or cross-neutralization**)
- 412-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG. Spear *et al.* [1993] (**complement**)

No. 464
MAb ID polyclonal
HXB2 Location gp160 (304–320)
Author Location gp120 (MN)
Epitope RKRIHIGPGRAFYTT
Neutralizing L (MN ALA-1)
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
References Spear *et al.* 1994

- 40% of antibody in serum that can bind to native viral proteins on MN-infected cells can be blocked by the peptide RKRIHIGPGRAFYTT, which can also block 75-95% of the complement activation on HIV infected cells. Spear *et al.* [1994]

No. 465
MAb ID CGP 47 439
HXB2 Location gp160 (304–322)
Author Location gp120
Epitope RKRIRIQRGPGRAFVTIGK?
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) human
Ab Type V3
References Jacobson 1998; Gauduin *et al.* 1998; Gunthard *et al.* 1994; Safrit *et al.* 1993; Liou *et al.* 1989

- CGP 47 439: Post-exposure passive transfer of murine BAT123 can confer protection to hu-PBL-SCID mice challenged with HIV-1 LAI – this protection is not elicited by CGP 47 439, suggesting that the protection is mediated by complement – the protective ability of BAT123 is lost when mice were treated with cobra venom factor, which inactivates serum complement – in this circumstance complement activation provided a protective advantage. Gauduin *et al.* [1998]
- CGP 47 439: Review of passive immunotherapy, summarizing Gunthard *et al.* [1994] in relation to other studies Jacobson [1998]. Gunthard *et al.* [1994]; Jacobson [1998]
- CGP 47 439: Phase I/IIA clinical trial studying multidose tolerability, immunogenicity and pharmacokinetic responses – GP 47 439 was well tolerated, serum t_1/2 was 8-16 days, and a virus burden reduction was noted in some patients. Gunthard *et al.* [1994]
- CGP 47 439: passive transfer to Hu-PBS-SCID mice confers protection against challenge with homologous cell-free virus – CGP 47 439 is a BAT123-human Ig chimera. Safrit *et al.* [1993]

No. 466
MAb ID polyclonal
HXB2 Location gp160 (304–322)
Author Location (MN)
Epitope RKRIHIGPGRAFYTTKN
Subtype multiple
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
References Cheingsong-Popov *et al.* 1992

- The Ab response of 829 HIV-1 infected subjects from eight geographic areas to a set of different V3 peptides was determined by ELISA and cross-inhibition studies – the Ab binding pattern was highly variable, depended on the geographic origin of the sample – 297 sera were tested in a neutralization assay – there was a correlation between Ab binding to the MN V3 loop and MN neutralizing titer, but with neutralization of IIIB or CBL-4. Cheingsong-Popov *et al.* [1992]

No. 467
MAb ID 178.1 (178.1.1)
HXB2 Location gp160 (305–309)
Author Location gp120 (305–309 BH10)
Epitope KSiRI
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* Env
Species (Isotype) mouse (IgG2a)
Ab Type V3
Research Contact C. Thiriart, Smith Kline and MRC AIDS reagent project
References Cook *et al.* 1994; Moore & Ho 1993; Back *et al.* 1993; Thiriart *et al.* 1989

- 178.1: UK Medical Research Council AIDS reagent: ARP331.
- 178.1: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro* – binding of GalCer to gp120 inhibited but did not completely block MAb binding. Cook *et al.* [1994]
- 178.1: gp41 amino acid substitutions 668 (N/S) and 675 (I/M) in gp41 interfere with 5023s neutralization potency, region 662-675 is ELDKWANLWNWFNI. Back *et al.* [1993]
- 178.1: Called 178.1.1 – conformational, does not bind well to denatured gp120. Moore & Ho [1993]
- 178.1: Reacts to gp120 and gp160 in RIPA EIA and immunoblot. Thiriart *et al.* [1989]

No. 468
MAb ID 257-D (257, 257-2-D-IV, 257-D-IV, 257, 257-2D, 257D, ARP3023)
HXB2 Location gp160 (305–309)
Author Location gp120 (MN)
Epitope KRIHI
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Zhang *et al.* 2002; Vella *et al.* 2002; York *et al.* 2001; Park *et al.* 2000; Nyambi *et al.* 2000; Oggioni *et al.* 1999; Beddows *et al.* 1999; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Stamatatos & Cheng-Mayer 1998; Gorny *et al.* 1998; Yang *et al.* 1998; LaCasse *et al.* 1998; Hioe *et al.* 1997b; Hill *et al.* 1997; Stamatatos *et al.* 1997; Schutten *et al.* 1997; Schutten *et al.* 1996; Wisnewski *et al.* 1996; Fontenot *et al.* 1995; Schutten *et al.* 1995b; Schutten *et al.* 1995a; Zolla-Pazner *et al.* 1995; D'Souza *et al.* 1995; Stamatatos & Cheng-Mayer 1995; VanCott *et al.* 1994; D'Souza *et al.* 1994; Spear *et al.* 1993; Cavacini *et al.* 1993a; Gorny *et al.* 1993; Karwowska *et al.* 1992b; D'Souza *et al.* 1991; Gorny *et al.* 1991
Keywords antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, assay development, binding affinity, co-receptor, complement, enhancing activity, inter-clade comparisons, kinetics, review, vaccine antigen design, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization

- 257-D: UK Medical Research Council AIDS reagent: ARP3023.
- 257-D: NIH AIDS Research and Reference Reagent Program: 1510.
- 257-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 257-D: Called 257: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides do not show as much ability to neutralize as V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. 257 was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 257-D: Called ARP3023: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. Vella *et al.* [2002] (**assay development**)
- 257-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002] (**variant cross-recognition or cross-neutralization**)
- 257-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3),

but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. York *et al.* [2001]

- 257-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 257-D showed intermediate reactivity. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 257-D: Called 257D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000]
- 257-D: rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 257-D bound rgp120 W61D but could only neutralize the W61D isolate following T-cell line adaptation. Beddows *et al.* [1999] (**vaccine antigen design**, **variant cross-recognition or cross-neutralization**, **vaccine-specific epitope characteristics**)
- 257-D: Study of a live-vector mucosal vaccine that expresses HIV-1 V3 domains using the bacterium Streptococcus gordonii which can express heterologous Ag and can colonize the oral cavity and vagina of mice – 268-D and 257-D recognized S. gordonii expressing the V3 domain of MN – the vaccine stimulated V3-specific IgG2a in mice. Oggioni *et al.* [1999] (**vaccine antigen design**)
- 257-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 257-D: MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 257-D: Kinetic parameters were measured, and the association rates were similar, but dissociation rate constants were quite variable for V3 MAbs, 257-D has a slow dissociation, thus the highest affinity among V3 MAbs. Gorny *et al.* [1998] (**kinetics**, **binding affinity**)
- 257-D: A T-cell line-adapted (TCLA) derivative of SI primary isolate 168P acquired the ability to be neutralized by anti-V3 MAbs – the primary isolate could use either CCR5 or CXCR4, and was not neutralized when infection was directed via either pathway, however the TCLA derivative uses CXCR4 only and is neutralized. LaCasse *et al.* [1998] (**co-receptor**, **variant cross-recognition or cross-neutralization**)
- 257-D: Called 257D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V3 MAbs 391-95D or 257D. Stamatatos & Cheng-Mayer [1998] (**vaccine antigen design**, **inter-clade comparisons**)
- 257-D: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. Yang *et al.* [1998] (**assay development**)
- 257-D: Called 257 – gp120 can inhibit MIP-1alpha from binding to CCR5, but this inhibitory effect is blocked by pre-incubation of gp120 with three anti-V3 MAbs: 447, 257, 1027 – MAb 670 which binds in the C5 region had no effect. Hill *et al.* [1997] (**antibody binding site definition and exposure**, **co-receptor**)
- 257-D: Neutralized (>90%) an SI-env chimeric virus and enhanced (>200%) an NSI-env chimeric virus. Schutten *et al.* [1997] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- 257-D: Binds less extensively than MAb 391-95D on the surface of HIV-1 isolates SF162 and SF128A – neutralizes less potently than 391-95D – stronger neutralization of primary macrophage targets than PBMC. Stamatatos *et al.* [1997] (**variant cross-recognition or cross-neutralization**)
- 257-D: IIIB neutralizing MAbs *in vitro* fail to neutralize in a mouse model *in vivo*. Schutten *et al.* [1996]
- 257-D: 257-D is V H5 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- 257-D: Called 257-D-IV – could neutralize MN and closely related JRCSF, but not 2 B subtype and 1 D subtype primary isolates in a multi-laboratory study involving 11 labs. D'Souza *et al.* [1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 257-D: Only inhibition of SI phenotype virus, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor. Schutten *et al.* [1995a] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- 257-D: Comparable affinity for SI and NSI viruses, in contrast to MAb MN215. Schutten *et al.* [1995b] (**variant cross-recognition or cross-neutralization**)
- 257-D: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V3 loop epitopes were less accessible to Ab binding on the virion surface than in the gp120 monomer, particularly for macrophage-tropic isolates SF162 and SF128a, relative to T-cell tropic SF2 – sCD4 association with gp120 better revealed this V3 epitope on TCLA SF2 and dual tropic (MU3) viruses than on macrophage tropic isolates. Stamatatos & Cheng-Mayer [1995] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 257-D: In serotyping study using flow-cytometry, bound only to virus with KRIHI. Zolla-Pazner *et al.* [1995] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 257-D: Included a multi-lab study for antibody characterization and assay comparison – best NAb against MN, but not IIIB.

D'Souza *et al.* [1994] (**variant cross-recognition or cross-neutralization**)
- 257-D: Potent MN neutralization, slow dissociation constant. VanCott *et al.* [1994] (**binding affinity**)
- 257-D: Additive MN or SF2 neutralization when combined with CD4 binding site MAb F105 – does not neutralize RF. Cavacini *et al.* [1993a] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 257-D: Neutralizes MN – binds SF2: epitope KSIYI – specificity: MN, SF2, NY5, RF. Gorny *et al.* [1993] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 257-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG – complement mediated virolysis of MN, but not in the presence of sCD4. Spear *et al.* [1993] (**complement**)
- 257-D: Reacts with MN, NY5, CDC4 and SF2, does not cross-react with RF, WM52, or HXB2. Karwowska *et al.* [1992b] (**variant cross-recognition or cross-neutralization**)
- 257-D: Called 257-2-D-IV – potent neutralizing MAb. D'Souza *et al.* [1991]

No. 469
MAb ID 311-11-D (311-11D, 311, 311D, 311-D)
HXB2 Location gp160 (305–313)
Author Location gp120 (MN)
Epitope KRIHIGP
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Gorny *et al.* 1998; Spear *et al.* 1993; Gorny *et al.* 1993; Gorny *et al.* 1991
Keywords antibody binding site definition and exposure, antibody generation, complement, inter-clade comparisons, review

- 311-11-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 311-11-D: Called 311: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides do not neutralize as well as V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. 311 was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 311-11-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 311-11-D showed weak reactivity. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 311-11-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 311-11-D: MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 311-11-D: Neutralizes MN – binds SF2: KSIYIGP. Gorny *et al.* [1993] (**antibody binding site definition and exposure**, **antibody generation**)
- 311-11-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG. Spear *et al.* [1993] (**complement**)

No. 470
MAb ID 41148D
HXB2 Location gp160 (305–313)
Author Location gp120 (MN)
Epitope KRIHIGP
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type V3
References Gorny & Zolla-Pazner 2004; Alsmadi & Tilley 1998; Pinter *et al.* 1993b
Keywords ADCC, review, variant cross-recognition or cross-neutralization

- 41148D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. 4117C and 41148D are anti-V3 MAbs that neutralize TCLA strains. Gorny & Zolla-Pazner [2004] (**review**)
- 41148D: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against strains IIIB, MN, SF-2, comparable to 4117C, however 41148D is 10x less efficient at neutralization, showing ADCC and neutralization don't always correlate. Alsmadi & Tilley [1998] (**ADCC**)
- 41148D: Neutralizes less potently than 4117C, reacts with MN, IIIB, SF2. Pinter *et al.* [1993b] (**variant cross-recognition or cross-neutralization**)

No. 471
MAb ID 391/95-D (391-95D, 391.5, 391/95D, 391/95)
HXB2 Location gp160 (305–318)
Author Location gp120 (MN)
Epitope KRIHIGPGRAFY
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)

References McCaffrey *et al.* 2004; Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Zhang *et al.* 2002; Lawson *et al.* 2002; Guillon *et al.* 2002b; Park *et al.* 2000; Ly & Stamatatos 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Stamatatos & Cheng-Mayer 1998; Stamatatos *et al.* 1997; Seligman *et al.* 1996; Stamatatos & Cheng-Mayer 1995; Fontenot *et al.* 1995; Gorny *et al.* 1993; Gorny *et al.* 1991

Keywords acute infection, antibody binding site definition and exposure, co-receptor, enhancing activity, inter-clade comparisons, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- 391/95-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 391/95-D: Called 391/95: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides do not show as much ability to neutralize as V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. 391/95 was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 391/95-D: Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The loss of any of the five glycans, within the V3 loop (GM299 V3), C2 (GM292 C2), C3 (GM329 C3), C4 (GM438 C4), or V5 (GM454 V5) made SF162 become sensitive to 391/95-D; SF162 is resistant to 391/95-D neutralization. V3 glycans tended to shield V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans shielded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 391/95-D: The affect of Ab binding on infectivity was studied by pseudotyping three related envs with different phenotypes – R5 viruses were preferentially enhanced, not X4 – the V3 region was the main determinant of Ab-mediated enhancement and modulation of the interaction between CCR5 and gp120 is critical – tests with MAbs anti-V3 391/95-D and CD4BS-specific GP68 indicate that Ab specificity did not determine whether or not infectivity was enhanced or neutralized, rather the phenotype was determined by Env conformation. Guillon *et al.* [2002b] (**co-receptor**, **enhancing activity**)
- 391/95-D: The phenotype and genotype of viral env sequences were studied over a period of seroconversion in one individual – Env trans-complementation demonstrated infectivity of clones derived pre-seroconversion were not influenced by MAb 391/95-D, but post-seroconversion clones were enhanced in the presence of 391/95-D, although the V3 binding region was unchanged – a change in the CD4-binding site was observed (NL43 427 Glu–>Lys) to be present in the post-seroconversion 391/95-D enhanced clone (see Guillon *et al.* [2002b]) Lawson *et al.* [2002]. Guillon *et al.* [2002b]; Lawson *et al.* [2002] (**enhancing activity**, **acute infection**)
- 391/95-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 391/95-D: Called 391-95D – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. Ly & Stamatatos [2000] (**antibody binding site definition and exposure**)
- 391/95-D: Called 391/95D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000] (**antibody binding site definition and exposure**)
- 391/95-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 391/95-D: Called 391.5 – MAb peptide-reactivity pattern clustered with immunological related MAbs: 391.5, 412 and 418, all selected with MN V3 peptide – the core amino acids HIGPGR tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 391/95-D: Called 391-95D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V3 MAbs 391-95D or 257D. Stamatatos & Cheng-Mayer [1998] (**antibody binding site definition and exposure**, **inter-clade comparisons**)
- 391/95-D: Called 391-95D – binds more extensively than MAb 257-D on the surface of HIV-1 isolates SF162 and SF128A – neutralizes more potently than 257-D – stronger neutralization of primary macrophage targets than PBMC – binding post-gp120-sCD4 association related to anti-V3 Abs neutralizing

capacity. Stamatatos *et al.* [1997] (**variant cross-recognition or cross-neutralization**)

- 391/95-D: Competition ELISAs with serial deletions estimated the epitope to be KRIHIGPGRAFY – unconstrained peptide had higher affinity than cyclic. Seligman *et al.* [1996] (**antibody binding site definition and exposure**)
- 391/95-D: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V3 loop epitopes were less accessible to Ab binding on the virion surface than in the gp120 monomer, particularly for macrophage-tropic isolates SF162 and SF128a, relative to T-cell tropic SF2 – sCD4 association with gp120 better revealed this V3 epitope on macrophage tropic and dual tropic (MU3) viruses, but not in TCLA SF2. Stamatatos & Cheng-Mayer [1995] (**antibody binding site definition and exposure**)
- 391/95-D: Neutralizes MN – binds to SF2, not IIIB. Gorny *et al.* [1993]

No. 472
MAb ID Aw
HXB2 Location gp160 (305–320)
Author Location gp120 (Gun-1wt)
Epitope KSITIGPGRAFHAI
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* Gun-1 *HIV component:* V3
Species (Isotype) rat
Ab Type V3
References McKnight *et al.* 1995

- Aw: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – Aw gives weak neutralization of both wildtype and v strains. McKnight *et al.* [1995]

No. 473
MAb ID Bw
HXB2 Location gp160 (305–320)
Author Location gp120 (Gun-1wt)
Epitope KSITIGPGRAFHAI
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* Gun-1 *HIV component:* V3
Species (Isotype) rat
Ab Type V3
References McKnight *et al.* 1995

- Bw: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – Bw gives weak neutralization of only the wildtype strain, does not bind to variant. McKnight *et al.* [1995]

No. 474
MAb ID DO142-10 (DO 142-10)
HXB2 Location gp160 (305–320)
Author Location gp120 (MN)
Epitope KRIHIGPGRAFYTT
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type V3
References Gorny & Zolla-Pazner 2004; Kwong *et al.* 2002; Sullivan *et al.* 1998a; Parren *et al.* 1998a; Parren & Burton 1997; Parren *et al.* 1997b; Ditzel *et al.* 1997; Seligman *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, binding affinity, enhancing activity, review, variant cross-recognition or cross-neutralization

- DO124-10: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. DO124-10 neutralizes some TCLA strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- D0124-10: Called D0124. Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- DO142-10: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different that Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**variant cross-recognition or cross-neutralization**, **binding affinity**)
- DO124-10: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab Ab fragment DO124-10 also enhances YU2 entry, ruling

out Fc interactions or Env cross-linking as a mechanism – while DO124-10 enhances YU2 entry 6-fold, it neutralizes HXBc2 under identical conditions. Sullivan *et al.* [1998a] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- DO142-10: Phage expression libraries panned against MN peptide were used to select Fab DO142-10 – Fab binds MN gp120, but not a primary isolate rec gp120. Ditzel *et al.* [1997] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- DO142-10: Neutralizes TCLA strains but not primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- DO142-10: Binds to gp120 MN and an MN V3 peptide with equal affinity, but binds a consensus B peptide and JRCSF less well, and to IIIB gp120 not at all. Parren & Burton [1997] (**variant cross-recognition or cross-neutralization**, **binding affinity**)
- DO142-10: Fab fragment – competition ELISAs with serial deletions defined the epitope KRIHIGPGRAFYTT. Seligman *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**)

No. 475
MAb ID Dv
HXB2 Location gp160 (305–320)
Author Location gp120 (Gun-1v)
Epitope KSITIGSGRAFHAI
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* Gun-1 *HIV component:* V3
Species (Isotype) rat
Ab Type V3
References McKnight *et al.* 1995

- Dv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype. McKnight *et al.* [1995]

No. 476
MAb ID Fv
HXB2 Location gp160 (305–320)
Author Location gp120 (Gun-1v)
Epitope KSITIGSGRAFHAI
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* Gun-1 *HIV component:* V3
Species (Isotype) rat
Ab Type V3
References McKnight *et al.* 1995

- Fv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype. McKnight *et al.* [1995]

No. 477
MAb ID Gv
HXB2 Location gp160 (305–320)
Author Location gp120 (Gun-1v)
Epitope KSITIGSGRAFHAI
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* Gun-1 *HIV component:* V3
Species (Isotype) rat
Ab Type V3
References McKnight *et al.* 1995

- Gv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype. McKnight *et al.* [1995]

No. 478
MAb ID Hv
HXB2 Location gp160 (305–320)
Author Location gp120 (Gun-1v)
Epitope KSITIGSGRAFHAI
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* Gun-1 *HIV component:* V3
Species (Isotype) rat
Ab Type V3
References McKnight *et al.* 1995

- Hv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype. McKnight *et al.* [1995]

No. 479
MAb ID polyclonal
HXB2 Location gp160 (305–322)
Author Location gp140 (SF162)
Epitope KSITIGPGRAFYATGD
Neutralizing yes
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade SF162 *HIV component:* gp140 *Adjuvant:* MF59
Species (Isotype) macaque, rabbit (IgG)
Ab Type V3
References Barnett *et al.* 2001

- SF162ΔV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization – when incorporated into a codon-optimized DNA vaccine with a CMV promoter, delivered by gene gun, SF162Δ2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162ΔV2, but not intactSF162, was used as the immunogen – NAbs titers specific for SF162 increased with multiple immunizations, while titers for non-homologous isolates decreased, but anti-V3 peptide binding Abs were not likely the source of this distinction because anti-V3 titers were much lower than those against the entire envelope, and the second booster immunization did not increase the titer of anti-V3 loop Abs. Barnett *et al.* [2001]

No. 480

MAb ID 50.1 (R/V3-50.1, Fab 50.1)
HXB2 Location gp160 (306–310)
Author Location gp120 (MN)
Epitope RIHIG
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN
HIV component: V3
Species (Isotype) mouse (IgG1κ)
Ab Type V3
Research Contact Mary White-Scharf, Repligen Corporation, Cambridge, MA
References Zhang *et al.* 2002; York *et al.* 2001; Park *et al.* 2000; Hoffman *et al.* 1999; Stanfield *et al.* 1999; LaCasse *et al.* 1998; Berman *et al.* 1997; Seligman *et al.* 1996; Fontenot *et al.* 1995; VanCott *et al.* 1995; Moore *et al.* 1994b; Robert-Guroff *et al.* 1994; VanCott *et al.* 1994; Bou-Habib *et al.* 1994; Rini *et al.* 1993; Ghiara *et al.* 1993; Potts *et al.* 1993; White-Scharf *et al.* 1993; D'Souza *et al.* 1991

- 50.1: NIH AIDS Research and Reference Reagent Program: 1289.
- 50.1: Called R/V3-50.1 – A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002]
- 50.1: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – the dissociation constant, Kd of 50.1 for the cell associated primary and TCLA Envs was equal, 7nM. York *et al.* [2001]
- 50.1: Called R/V3-50.1 – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes – 50.1 could only neutralize the sensitive form. Park *et al.* [2000]
- 50.1: The crystal structure of V3 loop peptides bound to Fabs was obtained – conformational changes in the tip of the V3 loop (GPGR) were observed when different Fabs were bound. Stanfield *et al.* [1999]
- 50.1: A T-cell line-adapted (TCLA) derivative of SI primary isolate 168P acquired the ability to be neutralized by anti-V3 MAbs – the primary isolate could use either CCR5 or CXCR4, and was not neutralized when infection was directed via either pathway, however the TCLA derivative uses CXCR4 only and is neutralized. LaCasse *et al.* [1998]
- 50.1: Binds to 6/7 isolates from breakthrough cases from a MN gp120 vaccine trial. Berman *et al.* [1997]
- 50.1: Competition ELISAs with serial deletions produced comparable estimate of epitope length to crystal structure and alanine substitution – KRIHIGP. Seligman *et al.* [1996]
- 50.1: Used to monitor HIV-1 Env expression in infected H9 cells. VanCott *et al.* [1995]
- 50.1: No neutralization of primary isolate JR-CSF – greater affinity for and neutralization of T cell tropic strain T-CSF, derived from JR-CSF. Bou-Habib *et al.* [1994]
- 50.1: Shows modest cross-reactivity among B clade gp120s, little outside B clade. Moore *et al.* [1994b]
- 50.1: Chimeric MN V3 loop in an HXB2 background allows increased FACS signal, Ab affinity, and viral neutralization. Robert-Guroff *et al.* [1994]
- 50.1: Potent MN neutralization, slow dissociation rate. VanCott *et al.* [1994]
- 50.1: Crystal structure of a 24 amino acid peptide from the V3 loop bound to 59.1 and 50.1 Fab fragments – epitope KRIHIGP. Ghiara *et al.* [1993]
- 50.1: No synergistic neutralization of MN when combined with CD4BS MAb F105 – isotype stated to be IgG2a. Potts *et al.* [1993]
- 50.1: Crystal structure of V3 loop bound to 50.1 – light chain binds just to the left of GPG, heavy chain binds further to the left. Rini *et al.* [1993]
- 50.1: Epitope defined by peptide reactivity and changes affinity with amino acid substitutions – epitope RIHIGP. White-Scharf *et al.* [1993]
- 50.1: Called R/V3-50.1 – potent neutralizing of lab strains. D'Souza *et al.* [1991]

No. 481
MAb ID
HXB2 Location gp160 (306–322)
Author Location gp160
Epitope RIRPGRAFVTIGK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: influenza *Strain:* B clade IIIB
HIV component: V3
Species (Isotype) human (IgA, IgG)
Ab Type V3
References Garulli *et al.* 2004
Keywords mucosal immunity

- Progesterone-treated BALB/c mice were intravaginally infected with recombinant influenza A virus (Flu/P18IIIB), expressing the immunodominant CTL epitope (P18IIIB, RIRPGRAFVTIGK, H-2Dd). A second immunization administered 2 weeks after the first doubled serum IgG levels and enabled detection of vaginal IgG. Low levels of vaginal IgA were detected in some animals. Garulli *et al.* [2004] (**mucosal immunity**)

No. 482
MAb ID BAT123 (BAT-123, CGP 47 439)

HXB2 Location gp160 (306–322)
Author Location gp120 (308–322 HXB2)
Epitope RIRIQRGPGRAFVTIGK
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1κ)
Ab Type V3
Research Contact Tanox Biosystems Inc and David Ho, ADARC, NY
References Gauduin *et al.* 1998; Parren *et al.* 1998a; Andrus *et al.* 1998; Poignard *et al.* 1996a; Sattentau & Moore 1995; Gauduin *et al.* 1995; Pirofski *et al.* 1993; Thali *et al.* 1993; Safrit *et al.* 1993; Moore & Ho 1993; Fung *et al.* 1990; Liou *et al.* 1989; Fung *et al.* 1987

- BAT123: CGP 47 439 is a BAT123 chimera that has a human IgG1 Fc domain.
- BAT123: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection. Andrus *et al.* [1998]
- BAT123: Post-exposure passive transfer of murine BAT123 can confer protection to hu-PBL-SCID mice challenged with HIV-1 LAI – this protection is not elicited by CGP 47 439, a BAT123 chimera that has a human IgG1 Fc domain, suggesting that the protection is mediated by complement – the protective ability of BAT123 is lost when mice were treated with cobra venom factor, which inactivates serum complement – IgG1 does not fix complement efficiently so an IgG2 MAb might perform better. Gauduin *et al.* [1998]
- BAT123: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- BAT123: Epitope described as RGPGRAFVTIGK – V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus (BAT123 less so than the others), mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs. Poignard *et al.* [1996a]
- BAT123: Passive transfer of BAT123 to hu-PBL-SCID mice 1 hour prior to inoculation with HIV-1 LAI, or up to four hours post-exposure, could protect mice from infection – the protection, like the MAb, was specific for the viral strain LAI. Gauduin *et al.* [1995]
- BAT123: Binds with high affinity to monomer and oligomer, rapid association and potent neutralization of lab strain. Sattentau & Moore [1995]
- BAT123: Called BAT-123 – conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120 – does not inhibit HIV-1 sera from binding to IIIB gp120. Moore & Ho [1993]
- BAT123: Variable region sequenced – heavy chain: V 3660-SB32, D unknown, J H3 – light chain: V kappa21, J kappa2. Pirofski *et al.* [1993]
- BAT123: Passive transfer to Hu-PBS-SCID mice confers protection against challenge with homologous cell-free virus. Safrit *et al.* [1993]
- BAT123: Anti-idiotypic MAb, AB19-4i, stimulates anti-anti-ID which neutralizes MN and IIIB. Fung *et al.* [1990]

No. 483
MAb ID 838-D (838)
HXB2 Location gp160 (307–311)
Author Location Env (RF)
Epitope KSITK
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Zhang *et al.* 2002; He *et al.* 2002; Nyambi *et al.* 2000; Gorny *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Nyambi *et al.* 1998; Hioe *et al.* 1997b; Gorny *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 838-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 838-D: Called 838: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 838-D: Called 838 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. He *et al.* [2002]
- 838-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2

are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002]

- 838-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7-10 fold preference for the oligomer. Gorny *et al.* [2000] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 838-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 838-D showed intermediate reactivity. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 838-D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to many A, B, C and F peptides, poor binding to D and E. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 838-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 838-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 838-D bound B clade virions but had limited cross-reactivity with other clades, with low levels of binding to A and D virions. Nyambi *et al.* [1998] (**inter-clade comparisons**)
- 838-D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 838-D was cross-reactive with V3 peptides from clade A and C, and could bind to 5/8 B clade V3 peptides – 50% neutralization of RF was obtained. Gorny *et al.* [1997] (**antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 838-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)

No. 484
MAb ID 1006-15D (1006)
HXB2 Location gp160 (307–312)
Author Location gp120 (RF)
Epitope KSITKG
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; He *et al.* 2002; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Gorny *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review

- 1006-15D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 1006-15D: Called 1006-15: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 1006-15D: Called 1006 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. He *et al.* [2002]
- 1006-15D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1006-15D showed strong cross-reactivity. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 1006-15D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to several B and F peptides, one C peptide, and some reactivity with A peptides – no binding was observed with D and E peptides. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 1006-15D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 1006-15D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – was somewhat cross-reactive with V3 peptides from clade A, C and other B clade V3 peptides, but not E

clade. Gorny *et al.* [1997] (**antibody generation**, **inter-clade comparisons**)

No. 485
MAb ID 782-D (782)
HXB2 Location gp160 (307–312)
Author Location Env (RF)
Epitope KSITKG
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Hioe *et al.* 1997b; Gorny *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 782-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 782-D: Called 782: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 782-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 782-D showed intermediate reactivity. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 782-D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to several B and F peptides, one C peptide, and some reactivity with A and D peptides. Zolla-Pazner *et al.* [1999a] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**)
- 782-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 782-D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 782-D was not cross-reactive with V3 peptides from clade A or E, but could bind to 3/8 B clade V3 peptides, and 1/2 C clade V3 peptides – 50% neutralization of RF was obtained. Gorny *et al.* [1997] (**antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 782-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)

No. 486
MAb ID 908-D (908, 908-12D)
HXB2 Location gp160 (307–312)
Author Location gp120 (RF)
Epitope KSITKG
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Gorny *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review

- 908-D:This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 908-D: Called 908: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 908-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross -reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 908-D showed strong cross-reactivity, but achieved only 50% neutralization on 2/5 isolates tested. Nyambi *et al.* [2000] (**inter-clade comparisons**)

- 908-D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to several A, B, C and F peptides, and poor binding to E and D peptides. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 908-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 908-D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 908-D was not cross-reactive with V3 peptides from clade E, but could bind to 6/8 B clade V3 peptides, 2/4 A clade, and 1/2 C clade – 50% neutralization of RF was obtained. Gorny *et al.* [1997] (**antibody binding site definition and exposure**, **antibody generation**, **inter-clade comparisons**)

No. 487
MAb ID 1027-15D (1027, 1027-D, 1027D, 1027-15)
HXB2 Location gp160 (307–313)
Author Location Env (RF)
Epitope KSITKGP
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Zhang *et al.* 2002; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Gorny *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review

- 1027-15D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 1027-15S: Called 1027-15: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 1027-15D: Called 1027-D – A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002] (**antibody binding site definition and exposure**)
- 1027-15D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1027-15D showed strong cross-reactivity. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 1027-15D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed moderate binding to several B and F peptides, one C peptide, and was not reactivity with A, D and E peptides. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 1027-15D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 1027-15D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 1027-15D was not cross-reactive with V3 peptides from clade A or E, but could bind to 3/8 B clade V3 peptides, and 1/2 C clade V3 peptides. Gorny *et al.* [1997] (**antibody binding site definition and exposure**, **antibody generation**, **inter-clade comparisons**)

No. 488
MAb ID F19.26-4
HXB2 Location gp160 (307–319)
Author Location gp120 (312–324 LAI)
Epitope IRIQRGPGRAFVT
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG2aκ)
Ab Type V3
References Boudet *et al.* 1994

- F19.26-4: Strain specific – used to raise anti-idiotype antibodies. Boudet *et al.* [1994]

No. 489
MAb ID F19.48-3
HXB2 Location gp160 (307–319)
Author Location gp120 (312–324 LAI)
Epitope IRIQRGPGRAFVT
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG2aκ)
Ab Type V3
References Boudet *et al.* 1994

- F19.48-3: Strain specific – used to raise anti-idiotype antibodies. Boudet *et al.* [1994]

No. 490
MAb ID F19.57-11
HXB2 Location gp160 (307–319)
Author Location gp120 (312–324 LAI)
Epitope IRIQRGPGRAFVT
Subtype B
Neutralizing L (LAI)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp120
Species (Isotype) mouse (IgG1κ)
Ab Type V3
References Boudet *et al.* 1995; Boudet *et al.* 1994; Boudet *et al.* 1991

- F19.57-11: Anti-anti-idiotypic antibodies (Ab3) were raised in BALBc mice that had greater breadth of reactivity than the original F19.57-11 (Ab3 could also recognize 1282 and SF2, with aa TRK(R or S)IYIGPGRA(WY or FH)T) Boudet *et al.* [1995]
- F19.57-11: MAb F19.57-11 is strain specific for LAI – used to raise anti-idiotype rabbit antibodies (called 57-B Ab2) Boudet *et al.* [1994]

No. 491
MAb ID 13105100
HXB2 Location gp160 (307–320)
Author Location gp120 (HXB2)
Epitope IRIQRGPGRAFVTI
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: V3
Species (Isotype) mouse (IgG1)
Ab Type V3
Research Contact ABI, Columbia, MD
References Dairou *et al.* 2004
Keywords antibody binding site definition and exposure

- 13105100: This MAb was raised against the peptide IRIQRGPGRAFVTI, located within the V3 loop flanking the GPGR apical motif. Two MAbs were used to determine the photodamage location in HIV-1 Env induced by sulfonated anionic porphyrins. The negatively charged porphyrins interact with positive charge in the V3 loop. When light activated, they damage amino acid side chains in the C5 region of Env, as evidenced by inhibition of binding of C5 MAb 9201, but not V3 MAb 13105100. Anionic porphyrins could be used in targeted photodynamic decontamination of biological fluids, such as blood, killing HIV without disabling the function of desirable transfusion products. Dairou *et al.* [2004] (**antibody binding site definition and exposure**)

No. 492
MAb ID M77
HXB2 Location gp160 (307–320)
Author Location gp120 (IIIB)
Epitope IRIQRGPGRAFVTI
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
Ab Type V3
Research Contact Advanced BioScience Laboratories, Rockville, MD, commercial
References Gorny & Zolla-Pazner 2004; Finnegan *et al.* 2002; Denisova *et al.* 2000; Watkins *et al.* 1996; Denisova *et al.* 1996; Denisova *et al.* 1995; DeVico *et al.* 1995; Cook *et al.* 1994; Watkins *et al.* 1993; di Marzo Veronese *et al.* 1993; di Marzo Veronese *et al.* 1992; Pal *et al.* 1992
Keywords antibody binding site definition and exposure, escape, review, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization

- M77: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. M77 neutralizes some TCLA strains. Gorny & Zolla-Pazner [2004] (**review**)
- M77: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I and Cluster II MAbs required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor, binding to a fusion intermediate. Cluster I and II MAbs bound to gp120/gp41 complexes at the cell-to-cell contact interface, in contrast to M77 which bound to gp120 that was evenly dispersed over the target cell surface. Finnegan *et al.* [2002]
- M77: M77 is highly strain specific for IIIB, but anti-idiotypic Abs directed against M77 can in turn elicit an Ab response with expanded HIV cross-reactivity – this mechanism may serve to prolong the primary response and to counter-balance viral immune evasion by mutation. Denisova *et al.* [2000] (**variant cross-recognition or cross-neutralization**)
- M77: Used M77 bound to gp120 as an immunogen – analysis of polyclonal and monoclonal (62 MAbs were generated) response suggests the M77-gp120 immunogen generated MAbs to more linear epitopes than gp120 alone or gp120 bound to CD4. Denisova *et al.* [1996] (**vaccine-specific epitope characteristics**)
- M77: Native M77 is highly strain specific, and V3 binding is primarily dependent on its heavy chain – a light chain switched Fab version of M77 could recognize HIV-1 strains that had substitutions on the left side of the V3 loop – R in GPGR is likely to be critical for binding. Watkins *et al.* [1996] (**variant cross-recognition or cross-neutralization**)
- M77: Reacted with both reduced and non-reduced covalently cross-linked gp120-CD4 complex. DeVico *et al.* [1995] (**antibody binding site definition and exposure**)
- M77: Conformational rearrangements upon binding of M77 to gp120 generates novel epitopes called metatopes. Denisova *et al.* [1995]
- M77: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro*. Cook *et al.* [1994]
- M77: Stated to be a murine MAb – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – M77 neutralization

was only slightly reduced by this mutation. Watkins *et al.* [1993] (**escape**)
- M77: Antibody binding to viral isolates from IIIB infected lab worker followed through time – A to T substitution resulted in the loss of neutralization and native gp120 binding, but not peptide binding. di Marzo Veronese *et al.* [1993] (**escape**)
- M77: IIIB-specific MAb, immunoprecipitates deglycosylated form. di Marzo Veronese *et al.* [1992] (**variant cross-recognition or cross-neutralization**)

No. 493
MAb ID polyclonal
HXB2 Location gp160 (307–321)
Author Location gp120 (307–321)
Epitope IRIQRGPGRAFVTIG
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) chimpanzee
Ab Type V3
References Goudsmit *et al.* 1988
Keywords antibody binding site definition and exposure, autologous responses, variant cross-recognition or cross-neutralization

- By three months post infection, chimpanzees infected with four strains of HIV-1 developed perisistant Ab responses. The V3 loop was a critical binding domain for strain-specific NAbs in sera from the infected chimpanzees. Goudsmit *et al.* [1988] (**antibody binding site definition and exposure**, **autologous responses**, **variant cross-recognition or cross-neutralization**)

No. 494
MAb ID SP.BAL114
HXB2 Location gp160 (308–317)
Author Location gp120 (BAL)
Epitope SIHIGPGRAF
Neutralizing L
Immunogen
Species (Isotype) mouse (IgG2aκ)
Ab Type V3
References Arendrup *et al.* 1995

- Authors suggest that during *in vivo* immunoselection of escape virus, the V3 domain gains increasing resemblance to that of lab strains. Arendrup *et al.* [1995]

No. 495
MAb ID SP.SF2:104
HXB2 Location gp160 (308–317)
Author Location gp120 (SF2)
Epitope SIYIGPGRAF
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) (IgG2aκ)
Ab Type V3
References Arendrup *et al.* 1995; Arendrup *et al.* 1993

- SP.SF2:104: Authors suggest that during *in vivo* immunoselection of escape virus, the V3 domain gains increasing resemblance to lab strains. Arendrup *et al.* [1995]
- SP.SF2:104: Anti-V3 antibody that could neutralize primary virus isolated from a time point of neutralization resistance of autologous virus. Arendrup *et al.* [1993]

No. 496
MAb ID polyclonal
HXB2 Location gp160 (308–319)
Author Location gp120 (304–318 LAI)
Epitope RIHIGPGRAFYT
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG, IgM)
Ab Type V3
References Langedijk *et al.* 1995

- Polylconal sera from six individuals tested for reactivity against a panel of peptides based on autologous sequences provide evidence for immunological escape mutations in the tip of the V3 loop. Langedijk *et al.* [1995]

No. 497
MAb ID 19b
HXB2 Location gp160 (308–320)
Author Location gp120
Epitope -I----G--FY-T
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type V3
Research Contact James Robinson, University of Connecticut, Storrs
References Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Poignard *et al.* 2003; Kwong *et al.* 2002; Zhang *et al.* 2002; Schulke *et al.* 2002; Kolchinsky *et al.* 2001; Park *et al.* 2000; Binley *et al.* 1999; Trkola *et al.* 1998; Parren *et al.* 1998a; Mondor *et al.* 1998; Parren *et al.* 1997b; Boots *et al.* 1997; Ugolini *et al.* 1997; Fouts *et al.* 1997; Binley *et al.* 1997a; D'Souza *et al.* 1997; Trkola *et al.* 1996a; Wu *et al.* 1996; Gauduin *et al.* 1996; Sattentau *et al.* 1995; Moore & Ho 1995; Moore *et al.* 1995a; Moore *et al.* 1995b; Sattentau 1995; Moore *et al.* 1994a; Moore *et al.* 1994b; Scott *et al.* 1990
Keywords antibody binding site definition and exposure, antibody interactions, review, vaccine antigen design

- 19b: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 19b: This paper attempts to engineer a gp120 molecule that would focus the immune response onto the IgG1b12 epitope. Adding a glycosylation sequon (P313N) to the V3 loop knocked out binding to anti-V3 MAbs loop 2, 19b and 447-52-D. Pantophlet *et al.* [2003b] (**vaccine antigen design**)

- 19b: Virion capture assays are not a good predictor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – while b12 was potent at neutralizing the three primary virions JR-CSF, A DA, and 89.6, the Abs F105, 19b, and Fab b6 were overall very poor neutralizers. Poignard *et al.* [2003]
- 19b: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V3 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- 19b: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- 19b: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140. Schulke *et al.* [2002]
- 19b: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002]
- 19b: Mutations in two glycosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 19b. Kolchinsky *et al.* [2001]
- 19b: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form but 19b was an exception and required around 950 ng/ml to neutralize either form. Park *et al.* [2000]
- 19b: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999]
- 19b: Used as a control in this Hx10 binding and neutralizing MAb study because 19b does not bind to Hx10. Mondor *et al.* [1998]
- 19b: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- 19b: No detectable neutralizing activity among primary isolates with different co-receptor usage – some neutralization of TCLA strains. Trkola *et al.* [1998]
- 19b: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – 19b has an epitope involving the tip of the V3 loop, with 5 or 6 essential amino acids distributed within a 12 amino acid stretch – the previously determined binding site was confirmed -I—-G–FY-T and some tolerated variants described, the I can be I, V, or L, the Y can be Y, F, or W – probably a beta-turn is required for FY or FF binding, but WY in can bind with out the context of the turn. Boots *et al.* [1997]
- 19b: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – there were four sequences with variations in the defined epitope among the 9 isolates tested. D'Souza *et al.* [1997]
- 19b: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with

oligomeric Env binding – 19b bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997]
- 19b: Neutralizes TCLA strains but not primary isolates. Parren *et al.* [1997b]
- 19b: Viral binding inhibition by 19b was weakly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997]
- 19b: Not as effective as IgG1b12 at neutralization *ex vivo* of virus direct from plasma of HIV-1 infected individuals. Gauduin *et al.* [1996]
- 19b: Inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]
- 19b: MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 – binding of 19b blocks this inhibition. Wu *et al.* [1996]
- 19b: Binds to some gp120s from clades A,B,C,E, and F – weakly neutralized some B and one C clade virus. Moore *et al.* [1995b]
- 19b: Despite broad gp120 binding reactivity, not broadly neutralizing. Moore *et al.* [1995a]
- 19b: Review: more broadly cross-reactive than anti-V3 tip MAb 447-D. Moore & Ho [1995]
- 19b: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity. Sattentau *et al.* [1995]
- 19b: V3 loop binding MAb that is more broadly clade cross-reactive than most (binds to 19/29 clade B and 10/12 clade E gp120s) Moore *et al.* [1994b]
- 19b: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies. Moore *et al.* [1994a]

No. 498
MAb ID loop 2 (Loop 2, IgG1 Loop 2, loop2)
HXB2 Location gp160 (308–321)
Author Location gp120
Epitope SISGPGRAFYTG
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
Research Contact D. Burton, Scripps Research Institute, La Jolla, CA
References Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Sullivan *et al.* 1998a; Parren *et al.* 1998a; Mondor *et al.* 1998; Parren & Burton 1997; Parren *et al.* 1997b; Ugolini *et al.* 1997; Ditzel *et al.* 1997; Wu *et al.* 1996; Moore *et al.* 1994b; Barbas III *et al.* 1993
Keywords antibody generation, antibody interactions, antibody sequence, variable domain, binding affinity, co-receptor, inter-clade comparisons, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- loop 2: Also known as Loop 2, IgG1 Loop 2 was a obtained by engineering Fab loop2 into an IgG1 molecule. (**antibody generation**)
- loop 2: Called loop2. This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. loop 2 neutralizes some TCLA strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- loop 2: This paper attempts to engineer a gp120 molecule that would focus the immune response onto the IgG1b12 epitope. Adding a glycosylation sequon (P313N) to the V3 loop knocked out binding to anti-V3 MAbs loop 2, 19b and 447-52-D. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- loop 2: Called loop2. scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V3 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- loop 2: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope – binding affinity of divalent IgG1 loop 2 is only 2-fold greater than monovalent Fab loop 2, suggesting the IgG1 form may bind with only one arm. Parren *et al.* [1998a] (**binding affinity**)
- loop 2: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – loop 2 enhances YU2 at concentrations up to 20 ug/ml. Sullivan *et al.* [1998a]
- loop 2: Binds to gp120 from MN and SF2 but not LAI. Ditzel *et al.* [1997] (**variant cross-recognition or cross-neutralization**)
- loop 2: Epitope is suggested to be GPGRAF – binds to 10/17 US clade B monomeric gp120s – IgG1 form can neutralize MN and 2 primary isolates tested. Parren & Burton [1997]
- loop 2: Neutralizes TCLA strains but not primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- loop 2: Viral binding inhibition by loop 2 MAb or Fab was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997]
- loop 2: MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 – binding of loop 2 blocks this inhibition. Wu *et al.* [1996] (**co-receptor**)

- loop 2: Called Loop 2 – shows modest cross-reactivity among B clade gp120s, little outside B clade. Moore *et al.* [1994b] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- loop 2: Sequences of the heavy and light chain Fab variable regions were generated. Barbas III *et al.* [1993] (**antibody sequence, variable domain**)

No. 499
MAb ID 4G10
HXB2 Location gp160 (308–322)
Author Location gp120 (308–322 LAI)
Epitope RIQRGPGRAFVTGK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: HBcAg fusion *HIV component:* V3
Species (Isotype) mouse
Ab Type V3
Research Contact Dr. Albrecht von Brunn, Max-von-Pettenkofer-Institut, Ludwig-Maximilians-Universitat Munchen, Germany
References von Brunn *et al.* 1993

- 4G10: NIH AIDS Research and Reference Reagent Program: 2534.
- 4G10: A 25 amino acid V3-loop sequence fused to HBcAg enhanced V3 immunogenicity. von Brunn *et al.* [1993]

No. 500
MAb ID 5F7
HXB2 Location gp160 (308–322)
Author Location gp120 (308–322 LAI)
Epitope RIQRGPGRAFVTGK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: HBcAg fusion *HIV component:* V3
Species (Isotype) mouse
Ab Type V3
Research Contact Dr. Albrecht von Brunn, Max-von-Pettenkofer-Institut, Ludwig-Maximilians-Universitat Munchen, Germany
References von Brunn *et al.* 1993

- 5F7: NIH AIDS Research and Reference Reagent Program: 2533.
- 5F7: A 25 amino acid V3-loop sequence fused to HBcAg enhanced V3 immunogenicity. von Brunn *et al.* [1993]

No. 501
MAb ID G3-523
HXB2 Location gp160 (308–322)
Author Location gp120 (308–322)
Epitope RIQRGPGRAFVTIGK
Neutralizing
Immunogen
Species (Isotype) mouse
Ab Type V3
References Jagodzinski *et al.* 1996; Matsushita *et al.* 1988

- G3-523: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS inhibits G3-523 binding. Jagodzinski *et al.* [1996]

No. 502
MAb ID MN215
HXB2 Location gp160 (308–322)
Author Location gp120 (MN)
Epitope RIHIGPGRAFYTTKN
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type V3
References Gorny & Zolla-Pazner 2004; Schutten *et al.* 1995b
Keywords antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization

- MN215: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. MN215 neutralizes some TCLA strains. Gorny & Zolla-Pazner [2004] (**review**)
- MN215: Minimum epitope for MAB using the Dutch consensus is AFYTTGE, different than defined for MN – generated by EBV transformation of PBMC – displayed higher affinity for NSI than for SI glycoproteins – amino acids HIGP were essential for binding. Schutten *et al.* [1995b] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

No. 503
MAb ID Nea 9301
HXB2 Location gp160 (308–323)
Author Location gp120 (IIIB)
Epitope RIQRGPGRAFVTIGKI
Neutralizing
Immunogen
Species (Isotype) mouse
Ab Type V3
Research Contact Dupont, commercial
References Wagner *et al.* 1996

No. 504
MAb ID 4117C
HXB2 Location gp160 (309–315)
Author Location gp120
Epitope IXIGPGR
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Abraham Pinter, Public Health Research Institute, Newark, NJ, 07103. pinter@phri.org.
References Pinter *et al.* 2004; Gorny & Zolla-Pazner 2004; He *et al.* 2002; Alsmadi & Tilley 1998; Pinter *et al.* 1993b; Pinter *et al.* 1993a; di Marzo Veronese *et al.* 1993; Tilley *et al.* 1992; Tilley *et al.* 1991a

Keywords ADCC, antibody binding site definition and exposure, antibody interactions, review, variant cross-recognition or cross-neutralization

- 4117c: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. 4117C and 4118D are anti-V3 MAbs that neutralize TCLA strains. Gorny & Zolla-Pazner [2004] (**review**)
- 4117c: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12 which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. 5/6 anti-V3 MAbs, including 4117c, had similar binding affinity to soluble SF162 and JR-FL rgp120s, although the V3 loop differs at three positions (HigpgrafyTtgE for JR-FL and TigpgrafyAtgD for SF162). Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 4117C: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. He *et al.* [2002]
- 4117C: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against MN and SF2, but not IIIB and RF. Alsmadi & Tilley [1998] (**ADCC**, **variant cross-recognition or cross-neutralization**)
- 4117C: Neutralizes SF2 and MN synergistically combined with anti-CD4 binding site discontinuous MAb. Pinter *et al.* [1993a]; Tilley *et al.* [1992] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 4117C: Binds V3 loop – does not immunoprecipitate soluble gp120, does react with gp120 on intact virions. Pinter *et al.* [1993b] (**antibody binding site definition and exposure**)
- 4117C: Potent neutralizing activity against MN, SF-2, and NY-5 – synergy with CD4BS MAb 1125H. Tilley *et al.* [1991a] (**antibody binding site definition and exposure**, **antibody interactions**, **variant cross-recognition or cross-neutralization**)

No. 505
MAb ID 419-D (419, 419D)
HXB2 Location gp160 (309–315)
Author Location gp120 (MN)
Epitope IHIGPGR
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)

References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; He *et al.* 2002; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Nyambi *et al.* 1998; Hioe *et al.* 1997b; Fontenot *et al.* 1995; Spear *et al.* 1993; Gorny *et al.* 1993; Karwowska *et al.* 1992b

Keywords antibody binding site definition and exposure, complement, inter-clade comparisons, mimotopes, review, superinfection, variant cross-recognition or cross-neutralization

- 419-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 419-D: Called 419: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**mimotopes**, **superinfection**)
- 419-D: Called 419 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. He *et al.* [2002]
- 419-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 419-D showed intermediate reactivity, and no neutralization when tested against five strains – discrepancy between the epitope as described in earlier papers and as described here, KRIHIGP. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 419-D: Review of clade specificity and anti-V3 HIV-1-Abs – epitope is described as KRIHIGP. Zolla-Pazner *et al.* [1999a] (**antibody binding site definition and exposure**, **review**)
- 419-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 419-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 419-D bound to 3/4 B clade virions, and to D clade MAL. Nyambi *et al.* [1998] (**inter-clade comparisons**)
- 419-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster

II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)

- 419-D: Neutralizes MN – binds SF2: IYIGPGR. Gorny *et al.* [1993] (**variant cross-recognition or cross-neutralization**)
- 419-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG. Spear *et al.* [1993] (**complement**)
- 419-D: MN, NY5 and SF2 strain specific, does not cross-react with RF, CDC4, WM52 or HXB2. Karwowska *et al.* [1992b] (**variant cross-recognition or cross-neutralization**)

No. 506
MAb ID 453-D (453)
HXB2 Location gp160 (309–315)
Author Location gp120 (MN)
Epitope IHIGPGR
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Fontenot *et al.* 1995; VanCott *et al.* 1994; Gorny *et al.* 1993; Gorny *et al.* 1991
Keywords antibody binding site definition and exposure, binding affinity, inter-clade comparisons, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- 453-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**)
- 453-D: Called 453: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 453-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 453-D showed intermediate reactivity. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 453-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 453-D : MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group – MAb 268, with a previously defined core epitope identical to 453 (HIGPGR), was not part of this reactivity group, illustrating that context can be critical. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 453-D : Called 453, epitope described as KRIHIGPGR – the tip of the V3 loop was presented in a mucin backbone – higher valency correlates with stronger affinity constant. Fontenot *et al.* [1995] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 453-D: Moderate homologous neutralization, moderately slow dissociation rate. VanCott *et al.* [1994] (**binding affinity**)
- 453-D: Neutralizes MN – binds SF2: IYIGPGR – specificity: MN, SF2, NY5, RF. Gorny *et al.* [1993] (**antibody binding site definition and exposure**)

No. 507
MAb ID 504-D (504, 504-10D)
HXB2 Location gp160 (309–315)
Author Location gp120 (MN)
Epitope IHIGPGR
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Gorny *et al.* 1993
Keywords antibody binding site definition and exposure, inter-clade comparisons, review

- 504-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 504-D: Called 504: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 504-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 504-D showed weak reactivity. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 504-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a] (**review**)

- 504-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 504-D – Neutralizes MN – binds SF2: IYIGPGR. Gorny *et al.* [1993] (**antibody binding site definition and exposure**)

No. 508
MAb ID 83.1 (MAb 83.1)
HXB2 Location gp160 (309–315)
Author Location gp120 (SF2)
Epitope IYIGPGR
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN *HIV component:* V3
Species (Isotype) mouse (IgG1)
Ab Type V3
Research Contact Mary White-Scharf, Repligen Corporation, Cambridge, MA
References Binley *et al.* 1999; Keller & Arora 1999; Jelonek *et al.* 1999; Potts *et al.* 1993; White-Scharf *et al.* 1993

- 83.1: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999]
- 83.1: Maternally transferred anti-V3 loop MAb selectively inhibits the anti-V3 loop Ab component of the IgG response to rgp120 SF2 in 21 day old BALBc mice. Jelonek *et al.* [1999]
- 83.1: 19 day old mice injected with 83.1 have a shift in IgG1 response away from the V3 loop upon vaccination, without decreasing the total IgG anti-gp120 response, suggesting that prior treatment with a MAb can mask immunogenic sites and shift the immune response to vaccination. Keller & Arora [1999]
- 83.1: Study of synergism of neutralization and binding comparing F105 and sCD4 with the V3 MAbs: 50.1, 59.1, 83.1, and 58.2 – synergy was observed, and the data suggest that binding of one ligand (F105) can increase the binding of the second (e. g. V3 loop MAbs) due to conformational changes. Potts *et al.* [1993]
- 83.1: Neutralizes SF2. White-Scharf *et al.* [1993]

No. 509
MAb ID 5023B
HXB2 Location gp160 (309–316)
Author Location gp120 (309–316 BH10)
Epitope IQRGPGra
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10 *HIV component:* V3
Species (Isotype) mouse (IgG)
Ab Type V3
References Langedijk *et al.* 1991

- 5023B: Generation and fine mapping of murine MAbs. Langedijk *et al.* [1991]

No. 510
MAb ID F58/D1 (F58)
HXB2 Location gp160 (309–316)
Author Location gp120 (IIIB)
Epitope IxxGPGRA
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type V3
References Jackson *et al.* 1999; Millar *et al.* 1998; Moore *et al.* 1993b; Broliden *et al.* 1991; Akerblom *et al.* 1990

- F58/D1: A 17 amino acid MicroAB was made from the third complementarity-determining region of the heavy chain of MAb – F58 neutralized 5x's more efficiently in terms of mass than the original MAb, 32-fold less on a molar basis – neutralization does not involve initial attachment, but fusion and events in early infection. Jackson *et al.* [1999]
- F58/D1: The interaction of a 17-amino-acid neutralizing microantibody (MicroAB) based on F58 and HIV-1 env was studied by electrospray ionization mass spectrometry. Millar *et al.* [1998]
- F58/D1: Binding to native gp120 1-3 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. Moore *et al.* [1993b]

No. 511
MAb ID P1/D12
HXB2 Location gp160 (309–316)
Author Location gp120
Epitope IxxGPGRA
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG)
Ab Type V3
References Moore *et al.* 1993b; Akerblom *et al.* 1990

- P1/D12: Binding to native gp120 1-3 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. Moore *et al.* [1993b]

No. 512
MAb ID P4/D10 (P4D10)

HXB2 Location gp160 (309–316)
Author Location gp120
Epitope IxxGPGRA
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1κ)
Ab Type V3
References Schonning *et al.* 1999; Schonning *et al.* 1998; Jacobson 1998; Hinkula *et al.* 1994; Arendrup *et al.* 1993; Moore *et al.* 1993b; Marks *et al.* 1992; Broliden *et al.* 1991; Broliden *et al.* 1990; Akerblom *et al.* 1990

- P4/D10: Called P4D10 – the stoichiometry of MAb neutralization was tested and the data indicated that binding for neutralization was was incremental not all or none, i.e., each envelope oligomer binds a single MAb and each Env oligomer bound reduces the chances of infection – MAb BC1071 was used for virion quantification – P4D10 binds only to Env with a glycosylation site mutation at the base of the V3 loop A308T. Schonning *et al.* [1999]
- P4/D10: Review of passive immunotherapy, summarizing Hinkula *et al.* [1994] in relation to other studies Jacobson [1998]. Hinkula *et al.* [1994]; Jacobson [1998]
- P4/D10: Called P4D10 – In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, anti-V3 MAbs were found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan more efficiently than HIV-BRU – Ab binding site was suggested to be 314-323 of BRU. Schonning *et al.* [1998]
- P4/D10: Used for passive immunotherapy in four late-stage HIV-infected patients – the serum level of p24 did not decrease in any of these four – see also MAb F58/H3. Hinkula *et al.* [1994]
- P4/D10: Primary isolates from different time points from one individual were not susceptible to neutralization by P4/D10. Arendrup *et al.* [1993]
- P4/D10: Binding to native gp120 3 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. Moore *et al.* [1993b]
- P4/D10: Variable domain sequenced and is identical to F58/H3. Marks *et al.* [1992]
- P4/D10: Neutralizing and ADCC activity. Broliden *et al.* [1990]

No. 513
MAb ID IIIB-13 V3 (1044-13 IIIB-V3-13 1727)
HXB2 Location gp160 (309–317)
Author Location gp120 (308–316 IIIB)
Epitope IQRGPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (Isotype) mouse (IgG1)
Ab Type V3
References Zhang *et al.* 2002; Chakrabarti *et al.* 2002; Watkins *et al.* 1993; D'Souza *et al.* 1994; Laman *et al.* 1993; Laman *et al.* 1992

- IIIB-13 V3: Also known as 1044-13 and as IIIB-V3-13 (J. P. Moore, per. comm.)
- IIIB-13 V3: UK Medical Research Council AIDS reagent: ARP3046.
- IIIB-13 V3: NIH AIDS Research and Reference Reagent Program: 1727.
- IIIB-13 V3: Called 1727: Used as a standard for comparing immune responses to modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation – experiment showed enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. Chakrabarti *et al.* [2002]
- IIIB-13 V3: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002]
- IIIB-13 V3: Included in a panel of antibodies used in a multi-lab study for antibody characterization and assay comparison, some neutralization of strains other than IIIB. D'Souza *et al.* [1994]
- IIIB-13 V3: Called IIIB-V3-13 – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – IIIB-V3-13 neutralization was only slightly reduced by this mutation. Watkins *et al.* [1993]
- IIIB-13 V3: Neutralizes IIIB but not MN. Laman *et al.* [1992]

No. 514
MAb ID IIIB-34 V3 (IIIB-V3-34)
HXB2 Location gp160 (309–317)
Author Location gp120 (308–316 IIIB)
Epitope IQRGPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
Species (Isotype) mouse (IgG1)
Ab Type V3
References Laman *et al.* 1993; Laman *et al.* 1992

- IIIB-34 V3: UK Medical Research Council AIDS reagent: ARP3047.
- IIIB-34 V3: Called IIIB-V3-34 – IIIB strain specific neutralization – binding is reduced somewhat by DTT or SDS-DTT, enhanced by NP40, but binds to native and denatured gp120. Laman *et al.* [1993]
- IIIB-34 V3: Neutralizes IIIB but not MN – QXGPG are critical amino acids for binding by Pepscan analysis. Laman *et al.* [1992]

No. 515
MAb ID A47/B1
HXB2 Location gp160 (309–318)
Author Location gp120 (307–316 IIIB)

Epitope IQRGPGRAFV
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp120
Species (Isotype) mouse (IgG)
Ab Type V3
References Akerblom *et al.* 1990

No. 516
MAb ID D59/A2
HXB2 Location gp160 (309–318)
Author Location gp120 (307–316 IIIB)
Epitope IQRGPGRAFV
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp120
Species (Isotype) mouse (IgG)
Ab Type V3
References Akerblom *et al.* 1990

No. 517
MAb ID G44/H7
HXB2 Location gp160 (309–318)
Author Location gp120 (307–316 IIIB)
Epitope IQRGPGRAFV
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp120
Species (Isotype) mouse (IgG)
Ab Type V3
References Akerblom *et al.* 1990

No. 518
MAb ID MO96/V3 (M096, M096/V3)
HXB2 Location gp160 (309–318)
Author Location gp120 (309–318)
Epitope IQRGPGRAFV+AHCNISRAKW
Neutralizing
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
Ab Type V3
References Gorny & Zolla-Pazner 2004; Ohlin *et al.* 1992
Keywords antibody binding site definition and exposure, antibody generation, review

- M093/V3: Review. provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains; a subset can also neutralize some primary isolates. The three IgMs, M096, M097, and M099, are non-neutralizing. Gorny & Zolla-Pazner [2004] (**review**)
- M096/V3: Generated in response to IIIB Env 286-467 upon *in vitro* stimulation of uninfected-donor lymphocytes, and binds to two peptides: 309-318 + 329-338. Ohlin *et al.* [1992] (**antibody binding site definition and exposure**, **antibody generation**)

No. 519
MAb ID μ5.5 (5.5, mu5.5, Rmu5.5)
HXB2 Location gp160 (309–319)
Author Location gp120 (MN)
Epitope IHIGPGRAFYT
Neutralizing L P
Immunogen
Species (Isotype) mouse (IgG1κ)
Ab Type V3
References Okamoto *et al.* 1998; Maeda *et al.* 1992

- mu5.5: Rmu5.5 is a humanized antibody of mouse MAb m5.5 – neutralized primary isolates with similar V3 loops – passive transfer of MAb to SCID-hu or hu-PBL-SCID mice conferred protection. Okamoto *et al.* [1998]
- mu5.5: sCD4 causes loss of IIIB type-specificity for MAb 0.5beta, allowing binding and neutralization of MN, in contrast to MAb mu5.5. Maeda *et al.* [1992]

No. 520
MAb ID 268-D (268-11-D-IV, 268D, 268, 268-11D, 268-10D, MAb 268, 268-10-D, ARP)
HXB2 Location gp160 (310–315)
Author Location gp120 (MN)
Epitope HIGPGR
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Zhang *et al.* 2002; Vella *et al.* 2002; York *et al.* 2001; Park *et al.* 2000; Nyambi *et al.* 2000; Hioe *et al.* 2000; Laisney & Strosberg 1999; Oggioni *et al.* 1999; Beddows *et al.* 1999; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; LaCasse *et al.* 1998; Stamatatos *et al.* 1997; Hioe *et al.* 1997b; Wisnewski *et al.* 1996; McKeating *et al.* 1996; Fontenot *et al.* 1995; Zolla-Pazner *et al.* 1995; Stamatatos & Cheng-Mayer 1995; VanCott *et al.* 1994; Spear *et al.* 1993; Gorny *et al.* 1993; Karwowska *et al.* 1992b; D'Souza *et al.* 1991; Gorny *et al.* 1991
Keywords antibody binding site definition and exposure, review

- 268-D: UK Medical Research Council AIDS reagent: ARP3024.
- 268-D: NIH AIDS Research and Reference Reagent Program: 1511.
- 268-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, while many neutralize some TCLA strains, a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 268-D: Called 268: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4 induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides do not show as much ability to neutralize as V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. 268

was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)

- 268-D: Called ARP3024: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. Vella *et al.* [2002]
- 268-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera—2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5—thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002]
- 268-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – one of the TCLA V3 viruses 320SI-C3.3 shows reduced binding with this MAb, the sequence of the epitope in 320SI is HIGPGR and in 320SI-C3.3 is RIGPGR. York *et al.* [2001]
- 268-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – V3 MAbs 447-52-D and 268-10-D did not effect proliferation. Hioe *et al.* [2000]
- 268-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 268-D showed weak reactivity. Nyambi *et al.* [2000]
- 268-D: Called 268D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000]
- 268-D: rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 268-D bound rgp120 W61D but could only neutralize the W61D isolate following T-cell line adaptation. Beddows *et al.* [1999]
- 268-D: Called MAb 268 – To identify potential mimotopes of V3, a hexapeptide phage library was screened with MAb 268 – two hexamers were identified, HLGPGR or KAIHRI that bind to 268 with the same binding site as the V3 loop and inhibit 268 MN gp120 – KLH conjugated hexamer KAIHRI stimulates Abs in rabbits that cross-react with ML gp120. Laisney & Strosberg [1999]
- 268-D: Called 268-11D – Study of a live-vector mucosal vaccine that expresses HIV-1 V3 domains using the bacterium Streptococcus gordonii which can express heterologous Ag and can colonize the oral cavity and vagina of mice – 268-D and 257-D recognized S. gordonii expressing the V3 domain of MN – the vaccine stimulated V3-specific IgG2a in mice. Oggioni *et al.* [1999]
- 268-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a]
- 268-D: Peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group – MAb 453, with an identical core epitope to 268 based on prior experiments (HIGPGR), was not part of this reactivity group, illustrating that context can be critical. Zolla-Pazner *et al.* [1999b]
- 268-D: A T-cell line-adapted (TCLA) derivative of SI primary isolate 168P acquired the ability to be neutralized by anti-V3 MAbs – the primary isolate could use either CCR5 or CXCR4, and was not neutralized when infection was directed via either pathway, however the TCLA derivative uses CXCR4 only and is neutralized. LaCasse *et al.* [1998]
- 268-D: Poor reactivity against HIV-1 isolates SF162 and SF128A and no neutralization, in contrast to MAbs 391/95-D and 257-D. Stamatatos *et al.* [1997]
- 268-D: Failed to neutralize HXB2 and chimeric virus with gp120 from primary isolates in an HXB2 background. McKeating *et al.* [1996]
- 268-D: 268-D is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996]
- 268-D: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V3 loop epitopes were less accessible to Ab binding on the virion surface than in the gp120 monomer, particularly for macrophage-tropic isolates SF162 and SF128a, relative to T-cell tropic SF2 – sCD4 association with gp120 did not influence the binding of 268-D to virion-associated gp120, although sCD4 binding did alter epitope exposure for other anti-V3 MAbs. Stamatatos & Cheng-Mayer [1995]
- 268-D: Serotyping study using flow-cytometry, if H of HIGPGR was substituted in virus, 268-D did not bind. Zolla-Pazner *et al.* [1995]
- 268-D: Moderate dissociation rate and homologous neutralization titer. VanCott *et al.* [1994]
- 268-D: Neutralizes MN – binds SF2: YIGPGR – specificity: MN, SF2, NY5, RF, CDC4. Gorny *et al.* [1993]
- 268-D: Mediated deposition of complement component C3 on HIV infected cells, but not in the presence of sCD4. Spear *et al.* [1993]
- 268-D: Reacts with MN, NY5, CDC4, RF and SF2, does not cross-react with WM52 or HXB2. Karwowska *et al.* [1992b]

- 268-D: Called 268-11-D-IV – strain specific weakly neutralizing. D'Souza *et al.* [1991]

No. 521
MAb ID 386-D (386, 386-10D, 386D)
HXB2 Location gp160 (310–315)
Author Location gp120 (MN)
Epitope HIGPGR
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Fontenot *et al.* 1995; VanCott *et al.* 1994; Gorny *et al.* 1993; Karwowska *et al.* 1992b
Keywords antibody binding site definition and exposure, binding affinity, inter-clade comparisons, isotype switch, review

- 386-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 386-D: Called 386: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides do not show as much ability to neutralize as V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. 386 was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 386-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 386-D showed intermediate reactivity. Nyambi *et al.* [2000] (**isotype switch**, **inter-clade comparisons**)
- 386-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 386-D: Peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 386-D: Slow dissociation rate, potent homologous neutralization. VanCott *et al.* [1994] (**binding affinity**)
- 386-D: Neutralizes MN – binds SF2: YIGPGR – specificity: MN, SF2, NY5, RF, CDC4. Gorny *et al.* [1993] (**antibody binding site definition and exposure**)

No. 522
MAb ID 5042A
HXB2 Location gp160 (310–315)
Author Location gp120 (310–315 BH10)
Epitope QrGPGR
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10
HIV component: V3
Species (Isotype) mouse (IgG)
Ab Type V3
References Gorny *et al.* 1991; Langedijk *et al.* 1991

- 5042A: Generation and fine mapping of murine MAbs. Langedijk *et al.* [1991]

No. 523
MAb ID 5042B
HXB2 Location gp160 (310–315)
Author Location gp120 (310–315 BH10)
Epitope QRGPGr
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10
HIV component: V3
Species (Isotype) mouse (IgG)
Ab Type V3
References Langedijk *et al.* 1991

- 5042B: Generation and fine mapping of murine MAbs. Langedijk *et al.* [1991]

No. 524
MAb ID 418-D (418, 418D)
HXB2 Location gp160 (310–316)
Author Location gp120 (MN)
Epitope HIGPGRA
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Zhang *et al.* 2002; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Gorny *et al.* 1993; Karwowska *et al.* 1992b
Keywords antibody binding site definition and exposure, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 418-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 418-D: Called 418: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. 418 was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)

- 418-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002]
- 418-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 418-D showed intermediate reactivity. Nyambi *et al.* [2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 418-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 418-D: Called 418 – MAb peptide-reactivity pattern clustered with immunological related MAbs: 391.5, 412 and 418, all selected with MN V3 peptide – the core amino acids HIGPGR tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**)
- 418-D: Neutralizes MN, does not bind to SF2 or HXB2. Gorny *et al.* [1993] (**variant cross-recognition or cross-neutralization**)
- 418-D: MN strain specific, does not cross-react with SF2, NY5, RF, CDC4 WM52 or HXB2. Karwowska *et al.* [1992b] (**variant cross-recognition or cross-neutralization**)

No. 525
MAb ID 5021
HXB2 Location gp160 (310–316)
Author Location gp120
Epitope QrGPGRa
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10 *HIV component:* V3
Species (Isotype) mouse (IgG)
Ab Type V3
References Moore *et al.* 1993b; Langedijk *et al.* 1991; Durda *et al.* 1990; Durda *et al.* 1988

- 5021: Binding to native gp120 100-300 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. Moore *et al.* [1993b]
- 5021: Generation and fine mapping of murine MAbs. Langedijk *et al.* [1991]

No. 526
MAb ID 5025B
HXB2 Location gp160 (310–316)
Author Location gp120 (310–316 BH10)
Epitope QRGPGra
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10 *HIV component:* V3
Species (Isotype) mouse (IgG)
Ab Type V3
References Langedijk *et al.* 1991

- 5025B: Generation and fine mapping of murine MAbs. Langedijk *et al.* [1991]

No. 527
MAb ID 5042
HXB2 Location gp160 (310–316)
Author Location gp120
Epitope QRGPGRA
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide
Species (Isotype) mouse
Ab Type V3
References Moore *et al.* 1993b; Durda *et al.* 1990; Durda *et al.* 1988

- 5042: Binding to native gp120 100-300 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. Moore *et al.* [1993b]

No. 528
MAb ID 110.3
HXB2 Location gp160 (310–317)
Author Location gp120 (308–328 BRU)
Epitope QRGPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1
Species (Isotype) mouse (IgG1κ)
Ab Type V3
References Connelly *et al.* 1994; Pirofski *et al.* 1993; Langedijk *et al.* 1992; Evans *et al.* 1989; Thomas *et al.* 1988

- 110.3: An anti-idiotypic MAb generated against 110.3 both mimics and binds to V3, suggesting that the V3 loop may associated with itself. Connelly *et al.* [1994]
- 110.3: MAb variable region sequenced – heavy chain: V 7138(40), D deletion, J H4 – light chain: V kappa21(47), J kappa2. Pirofski *et al.* [1993]
- 110.3: Included as a control. Evans *et al.* [1989]

No. 529
MAb ID 110.4
HXB2 Location gp160 (310–317)
Author Location gp120 (308–328 BRU)
Epitope QRGPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1
Species (Isotype) mouse (IgG1κ)
Ab Type V3

Research Contact Genetic Systems Corp, Seattle WA, E. Kinney-Thomas
References Guillerm *et al.* 1998; Cao *et al.* 1997b; Valenzuela *et al.* 1998; McDougal *et al.* 1996; Connelly *et al.* 1994; Boudet *et al.* 1994; Thali *et al.* 1994; Arendrup *et al.* 1993; Pirofski *et al.* 1993; Thali *et al.* 1993; Langedijk *et al.* 1992; Thali *et al.* 1992b; Callahan *et al.* 1991; Thomas *et al.* 1988
Keywords anti-idiotype, antibody binding site definition and exposure, antibody sequence, variable domain, escape

- 110.4: Used for flow cytometry in a study of the anti-CD4, CDR3 loop MAb called 13B8.2, in a study of HIV-1 induced programmed cell death. Guillerm *et al.* [1998]
- 110.4: Neutralization of LAI in CEM cells by anti-V3 MAbs 110.4 and N11-20 is through inhibition of viral binding to the cell. Valenzuela *et al.* [1998]
- 110.4: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4. Cao *et al.* [1997b] (**antibody binding site definition and exposure**)
- 110.4: Neutralizes HIV-1 LAI. McDougal *et al.* [1996]
- 110.4: An anti-idiotypic MAb generated against 110.3 also blocks binding of 110.4. Connelly *et al.* [1994] (**anti-idiotype**)
- 110.4: gp41 mutation that confers resistance to neutralization by anti-CD4 binding site antibodies does not reduce neutralizing efficiency of this V3 region MAb. Thali *et al.* [1994] (**antibody binding site definition and exposure**)
- 110.4: Primary isolates from different time points from one individual were not susceptible to neutralization by 110.4. Arendrup *et al.* [1993]
- 110.4: MAb variable region sequenced – heavy chain: V 3660-SB32, D closest to DSP2.3, 2.4 and .6, J H2 – light chain: V kappa21, J kappa2. Pirofski *et al.* [1993] (**antibody sequence, variable domain**)
- 110.4: 313 P/S substitution in the V3 region disrupts binding. Thali *et al.* [1992b] (**antibody binding site definition and exposure**, **escape**)
- 110.4: Polyanionic polysaccharides were proposed to inhibit viral functions such as binding and syncytia formation through interations mediated through the local high positive charge density in the V3 loop. The binding of this anti-V3 antibody is inhibited by dextransulfate. Callahan *et al.* [1991]

No. 530
MAb ID 110.5
HXB2 Location gp160 (310–317)
Author Location gp120 (308–328 BRU)
Epitope QRGPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1
Species (Isotype) mouse (IgG1κ)
Ab Type V3
Research Contact E. Kinney-Thomas or Genetic Systems, Seattle WA
References Parren *et al.* 1998a; Ugolini *et al.* 1997; Binley *et al.* 1997a; Jeffs *et al.* 1996; McDougal *et al.* 1996; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; Sattentau *et al.* 1995; Klasse *et al.* 1993a; Thali *et al.* 1993; Moore *et al.* 1993b; Pirofski *et al.* 1993; McKeating *et al.* 1992a; Langedijk *et al.* 1992; Sattentau & Moore 1991; Cordell *et al.* 1991; Moore *et al.* 1990; Thomas *et al.* 1988; Reitz *et al.* 1988

- 110.5: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- 110.5: Viral binding inhibition by 110.5 was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997]
- 110.5: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120. Jeffs *et al.* [1996]
- 110.5: Neutralizes HIV-1 LAI. McDougal *et al.* [1996]
- 110.5: Reciprocal binding inhibition with other anti-V3 MAbs – enhances binding of some anti-V2 MAbs – binding enhanced by some CD4 binding site MAbs. Moore & Sodroski [1996]
- 110.5: Did not induce dissociation of gp120, as sCD4 did – discrepancy with Poignard *et al.* [1996a], that was suggested to be due to MAb interference with detection, as the gp120-MAb complex was denatured in the Poignard study Moore *et al.* [1990]. Moore *et al.* [1990]; Poignard *et al.* [1996a]
- 110.5: V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus, mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs. Poignard *et al.* [1996a]
- 110.5: Pretreatment of HX10-infected H9 cells with sCD4 decreases signal from 110.5 at 37 degrees due to dissociation of gp120-gp41. Sattentau *et al.* [1995]
- 110.5: Binds with high affinity to monomer and oligomer, rapid association and potent neutralization of lab strains – neutralizes cell-free Hx10. Sattentau & Moore [1995]
- 110.5: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 110.5 is not affected. Klasse *et al.* [1993a]; Reitz *et al.* [1988]
- 110.5: Thrombin cleavage of V3 loop between R-315 and A-316 abrogates binding – can inhibit C4 region antibody which has conformational requirements (G3-299) – binding to native gp120 100-300 fold greater than to denatured. Moore *et al.* [1993b]
- 110.5: Variable region sequenced – heavy chain: V 3660-SB32, D closest to DSP2.3, 2.4 and .6, J H2 – light chain: V kappa21, J kappa2. Pirofski *et al.* [1993]
- 110.5: Binding insensitive to gp120 reduction. Cordell *et al.* [1991]
- 110.5: Two fold increase in binding to gp120 in the presence of bound sCD4. Sattentau & Moore [1991]

No. 531
MAb ID 58.2

HXB2 Location gp160 (310–317)
Author Location gp120 (MN)
Epitope HIGPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN
HIV component: V3
Species (Isotype) mouse (IgG1κ)
Ab Type V3
Research Contact Repligen Corp.
References York *et al.* 2001; Stanfield *et al.* 1999; Seligman *et al.* 1996; Moore *et al.* 1994b; Potts *et al.* 1993; White-Scharf *et al.* 1993

- 58.2: 58.2's epitope was noted to be IGPGRAF – Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. York *et al.* [2001]
- 58.2: The crystal structure of Fab 58.2 bound to V3 loop peptides was obtained – conformational changes in the tip of the V3 loop (GPGR) were observed when different MAbs were bound – 58.2's epitope was defined as KRKRIHIGPGRAFY. Stanfield *et al.* [1999]
- 58.2: Competition ELISAs with serial deletions produced longer estimates of epitope length, RIHIGPGRAFY, than Alanine substitution, suggesting significance of non-contact residues. Seligman *et al.* [1996]
- 58.2: Modest cross-reactivity among B clade gp120s, little outside B clade – core epitope as I-IHIG. Moore *et al.* [1994b]
- 58.2: Did not synergistically neutralize MN in combination with MAb F105 – there was synergistic neutralization when combined with sCD4. Potts *et al.* [1993]
- 58.2: Epitope defined by peptide reactivity and changes in affinity with amino acid substitutions – 4/7 primarily isolates were neutralized. White-Scharf *et al.* [1993]

No. 532
MAb ID polyclonal
HXB2 Location gp160 (310–318)
Author Location gp120
Epitope QRGPGRAFV?
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide keyhole limpet hemocyanin (KLH) conjugate, peptide Brucella abortus (Ba) conjugate, peptide lipopolysaccharide (LPS) conjugate *Strain:* B clade MN *HIV component:* V3
Species (Isotype) mouse (IgA, IgG1, IgG2a)
References Golding *et al.* 2002a

- Internasal (i.n.) immunization with V3-Ba induced mucosal anti-V3 NAbs and IFN-gamma secreting T cells – V3-Ba, V3-KLH and V3-LPS could each induce serum and mucosal IgA and IgG in BALB/c mice – i.n. plus i.p. immunizations gave higher titers than i.n. alone – the response to V3-KLH was mainly restricted to IgG1, and to V3-Ba, IgG2a – class II KO mice (CD4+-deficient) did not respond to V3-KLH, but did respond to V3-Ba, suggesting that V3-Ba may be effective in eliciting Ab responses in HIV-1 infected individuals that have impaired CD4+ T cell function. Golding *et al.* [2002a]

No. 533
MAb ID 537-D (537)
HXB2 Location gp160 (311–315)
Author Location gp120 (MN)
Epitope IGPGR
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Nyambi *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Fontenot *et al.* 1995; VanCott *et al.* 1994; Gorny *et al.* 1993; Gorny *et al.* 1992; Karwowska *et al.* 1992b
Keywords antibody binding site definition and exposure

- 537-D: Called 537: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 537-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 537-D showed weak reactivity. Nyambi *et al.* [2000]
- 537-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a]
- 537-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b]
- 537-D: Moderate homologous neutralization, relatively rapid dissociation constant. VanCott *et al.* [1994]
- 537-D: MN type specific neutralization observed – binds SF2, also IGPGR. Gorny *et al.* [1992, 1993]
- 537-D: Reacts with MN, NY5, CDC4, RF, WM52 and SF2, but does not cross-react with HXB2. Karwowska *et al.* [1992b]

No. 534
MAb ID 5020
HXB2 Location gp160 (311–316)
Author Location gp120 (311–316 BH10)
Epitope RGPGRA
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10
HIV component: V3

Species (Isotype) mouse (IgG)
Ab Type V3
References Langedijk *et al.* 1991

- 5020: Generation and fine mapping of murine MAbs. Langedijk *et al.* [1991]

No. 535
MAb ID RC25
HXB2 Location gp160 (311–316)
Author Location gp120 (JRFL)
Epitope IGPGRA
Subtype B
Neutralizing L
Immunogen
Species (Isotype) humanized mouse
Ab Type V3
References Kaizu *et al.* 2003; Kimura *et al.* 2002
Keywords co-receptor, HAART, ART

- RC25: MD14 is a R5X4 SHIV with a B clade Env; the V3 loop of an E-clade Env was inserted into MD14 to create SHIV-TH09V3, an R5 virus. SHIV-TH09V3 could infect both cynomolgous and pig-tailed macaques, and the R5 co-receptor usage was maintained after passage through macaques. The MAb RC25 recognized B clade V3 loops, and reacted with SHIV-MD14. Rabbit anti-sera raised against a NSI Clade E consensus preferentially recognized SHIV-TH09V3. Kaizu *et al.* [2003] (**co-receptor**)
- RC25: RC25 is a humanized MAb that recognizes the epitope IGPGRA – it has strong neutralizing activity against JRFL (R5 virus) and weak against NL4-3 (X4 virus) and is used as a control in a study of NAb activity in patients undergoing HAART. Kimura *et al.* [2002] (**HAART, ART**)

No. 536
MAb ID 5023A (5023, NEA-9205, NEA 9205)
HXB2 Location gp160 (311–317)
Author Location gp120 (311–317 BH10)
Epitope RgPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10 *HIV component:* V3
Species (Isotype) mouse (IgG)
Ab Type V3
Research Contact Paul Durda, Du Pont de Nemours and Co
References Schonning *et al.* 1998; Rovinski *et al.* 1995; Back *et al.* 1993; D'Souza *et al.* 1991; Langedijk *et al.* 1991

- 5023A: Called NEA-9205 – The N306 glycan of the V3 loop makes the tip of the V3 loop inaccessible to this MAb in oligomeric Env, loss of this glycan enhances neutralization sensitivity. Schonning *et al.* [1998]
- 5023A: Called 5023 in this paper – Used to precipitate gp160 in immunoblots in a study examining the feasibility of using unprocessed gp160 glycoprotein as an immunogen. Rovinski *et al.* [1995]
- 5023A: Called 5023 – Langedijk also has an MAb called 5023B – gp41 amino acid substitutions 668 (N/S) and 675 (I/M) in gp41 interfere with 5023s neutralization potency, region 662-675 is ELDKWANLWNWFNI. Back *et al.* [1993]
- 5023A: Called 5023 – Langedijk also has an MAb called 5023B – strong cross-reactive neutralizing MAb. D'Souza *et al.* [1991]
- 5023A: Generation and Fine mapping of murine MAbs. Langedijk *et al.* [1991]

No. 537
MAb ID 110.6
HXB2 Location gp160 (311–318)
Author Location gp120 (BRU)
Epitope RGPGRAFV
Neutralizing L (weak)
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1
Species (Isotype) mouse (IgG1λ)
Ab Type V3
References Langedijk *et al.* 1992; Pirofski *et al.* 1993; Thomas *et al.* 1988

- 110.6: Variable region sequenced – heavy chain: V J558-146b.1alpha, D closest to DSP16.2, J H3 – light chain: V lambda1, J lambda1. Pirofski *et al.* [1993]

No. 538
MAb ID polyclonal
HXB2 Location gp160 (311–318)
Author Location gp120 (MN)
Epitope IGPGRAFY
Neutralizing L
Immunogen Vaccine
Vector/Type: B. abortus complex *Strain:* B clade MN, B clade SF2 *HIV component:* gp120
Species (Isotype) mouse (IgG2a)
Ab Type V3
References Golding *et al.* 1995

- Ab is evoked even in mice depleted of CD4+ cells.

No. 539
MAb ID 10/36e
HXB2 Location gp160 (311–321)
Author Location gp120 (311–321 HXB10)
Epitope RGPGRAFVTIG
Neutralizing L (HXB10)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10 *HIV component:* gp120
Species (Isotype) rat (IgG2a)
Ab Type V3
References Peet *et al.* 1998; McKeating *et al.* 1993b; McKeating *et al.* 1992a

- 10/36e: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 10/36e binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]

- 10/36e: Binding to virion gp120 enhanced by sCD4. McKeating *et al.* [1992a]

No. 540
MAb ID 10/54 (10/54ow/6i/6i)
HXB2 Location gp160 (311–321)
Author Location gp120 (311–321 HXB10)
Epitope RGPGRAFVTIG
Neutralizing L (HXB10)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG1)
Ab Type V3
References Peet *et al.* 1998; McKeating *et al.* 1993b; McKeating *et al.* 1993a; McKeating *et al.* 1992a

- 10/54: Called 10/54ow/6i/6i: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 10/54 binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]
- 10/54: Studied in the context of a neutralization escape mutant. McKeating *et al.* [1993a]
- 10/54: Binding to virion gp120 enhanced by sCD4. McKeating *et al.* [1992a]

No. 541
MAb ID 11/85b (11/85b/14I/14I)
HXB2 Location gp160 (311–321)
Author Location gp120 (311–321 HXB10)
Epitope RGPGRAFVTIG
Neutralizing L (HXB2)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2b)
Ab Type V3
References McKeating *et al.* 1993b; McKeating *et al.* 1992a

- 11/85b: Binding to virion gp120 enhanced by sCD4. McKeating *et al.* [1992a]

No. 542
MAb ID polyclonal
HXB2 Location gp160 (311–322)
Author Location gp120 (MN)
Epitope IGPGRAFYTTKN
Neutralizing L (MN ALA-1)
Immunogen Vaccine
Vector/Type: human rhinovirus 14 *Strain:* B clade MN *HIV component:* V3
Species (Isotype) guinea pig
Ab Type V3
References Smith *et al.* 1998

- The tip of the MN V3 loop (IGPGRAFYTTKN) was inserted into cold-causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies – chimeric viruses elicited potent NAbs against ALA-1 and MN. Smith *et al.* [1998]

No. 543
MAb ID 0.5β (0.5 beta, 0.5beta)
HXB2 Location gp160 (311–324)
Author Location gp120 (316–330 HXB2)
Epitope RGPGRAFVTIGKIG
Subtype B
Neutralizing L (IIIB)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: Env
Species (Isotype) mouse (IgG1κ)
Ab Type V3
Research Contact Shuzo Matsushita or Toshio Hattori of Kumamoto University
References Harada *et al.* 2004; Kawai *et al.* 2003; Zvi *et al.* 2000; Tugarinov *et al.* 2000; Jagodzinski & Trzeciak 2000; Fortin *et al.* 2000; Tugarinov *et al.* 1999; Faiman & Horovitz 1997; Wyatt *et al.* 1997; Zvi *et al.* 1997; Huang *et al.* 1997; Faiman *et al.* 1996; Jeffs *et al.* 1996; McDougal *et al.* 1996; Warrier *et al.* 1996; Jagodzinski *et al.* 1996; Zvi *et al.* 1995a; Zvi *et al.* 1995b; Broder *et al.* 1994; Boudet *et al.* 1994; Okada *et al.* 1994; Thali *et al.* 1994; Cook *et al.* 1994; Watkins *et al.* 1993; Klasse *et al.* 1993a; Moore *et al.* 1993b; di Marzo Veronese *et al.* 1993; Sperlagh *et al.* 1993; McKeating *et al.* 1992a; Maeda *et al.* 1992; Emini *et al.* 1992; Matsushita *et al.* 1992; D'Souza *et al.* 1991; Nara *et al.* 1990; Reitz *et al.* 1988; Skinner *et al.* 1988a; Skinner *et al.* 1988b; Matsushita *et al.* 1988
Keywords anti-idiotype, antibody binding site definition and exposure, antibody generation, antibody interactions, brain/CSF, co-receptor, complement, escape, structure, variant cross-recognition or cross-neutralization

- 0.5beta: UK Medical Research Council AIDS reagent: ARP3025.
- 0.5beta: NIH AIDS Research and Reference Reagent Program: 1591.
- 0.5beta: Studies on the temperature dependence of infectious virus (increased temperatures up to 37 degress increases infectivity) showed that X4 pseudoviruses that were infectious at room temperature were also more resistant to anti-V3 0.5beta and anti-CXCR4 blocking peptide T140. This implies that virus more heavily populated with functional envelopes are more infectious. Harada *et al.* [2004] (**co-receptor**)
- 0.5beta: 0.5beta was used as a control for gp120 expression relative to Nef expression soon after infection of cultures. The goal of this study was to elicit anti-Nef IgM human Abs in trans-chromosome mice that carry human chromosomes responsible for Ig production. These mice were immunized with recombinant Nef protein. Human heavy chain, mouse light

chain anti-Nef IgM were obtained. The hope was that these human IgM anti-Nef chimeric Abs would activate complement mediated cytolysis; C3 deposition was induced but not at high enough levels to induce lysis. Kawai *et al.* [2003] (**complement**)

- 0.5beta: Host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5beta or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab. Fortin *et al.* [2000] (**antibody interactions**)
- 0.5beta: MAbs 0.5beta and G3-42 were used to study synthesis of oligomeric and monomeric forms of Env – inhibition of glycosylation by tunicamycin results in reduction of oligomeric gp120 at the cell surface and of monomer in the cytoplasm – neither MAb recognized non-glycosylated Env precursor. Jagodzinski & Trzeciak [2000]
- 0.5beta: 14/18 residues of peptide P1053, RKSIRIQRGPGRAFVTIG, were shown to be involved in the Ab recognition site using NMR – QRGPGR forms a beta-hairpin turn at the center of the binding pocket. Tugarinov *et al.* [2000] (**antibody binding site definition and exposure**)
- 0.5beta: NMR and mutation cycles were employed to generate a model of the peptide-antibody complex, showing aa residues that interact or do not contribute to the binding of MAb 0.5beta Fv with the peptide – F96(L) of 0.5beta binds to Pro13, H52(H) interacts with Ile7, Ile9, Gln10, and D56(H) interacts with Arg11 of the V3 loop peptide – RGPG retains hairpin conformation binds in the center of a groove. Zvi *et al.* [2000] (**structure**)
- 0.5beta: NMR structure reveals that Ab bound IIIB-V3 peptide adopts an unexpected type VI cis proline beta-turn. Tugarinov *et al.* [1999] (**structure**)
- 0.5beta: The Fv fragment was purified and the temperature dependence and effect of mutations was studied. Faiman & Horovitz [1997]
- 0.5beta: Relative to the native peptide, an O-linked alpha-galactosamine modified V3 peptide enhanced binding to 0.5 beta, while an N-linked beta-glucosamine modified peptide showed reduced binding. Huang *et al.* [1997] (**antibody binding site definition and exposure**)
- 0.5beta: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. Wyatt *et al.* [1997] (**antibody binding site definition and exposure**)
- 0.5beta: The structure of a 17 amino acid V3 peptide bound to the Fab was studied using NMR. Zvi *et al.* [1997] (**structure**)
- 0.5beta: For Fv fragment of 0.5beta, the combined variable regions of the heavy and light chain residues, were purified. Binding of the V3 peptide epitope TRKSIRIQRGPGRAFVTIGK was studied through mutagenesis of arginines and the free energy of binding in various salt concentrations. R4A, R8A, and R11A all reduce the free energy; R8 is embedded in the peptide-Fv fragment, while R11 is more solvent exposed. Faiman *et al.* [1996] (**antibody binding site definition and exposure**)
- 0.5beta: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS inhibits 0.5beta binding – 0.5beta epitope described as GPGRAFVTIG. Jagodzinski *et al.* [1996]
- 0.5beta: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120. Jeffs *et al.* [1996] (**antibody binding site definition and exposure**)
- 0.5beta: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. Warrier *et al.* [1996] (**antibody interactions**)
- 0.5beta: The interactions of the peptide RKSIRIQRGPGRAFVT 0.5beta were studied by NMR, and hydrophobic interactions between the two Is and the V form the base of a 12 amino acid loop with GPGR at the apex. Zvi *et al.* [1995b] (**antibody binding site definition and exposure**)
- 0.5beta: NMR of 0.5beta bound NNTRKSIRIQRGPGRAFVTIGKIG suggests that the bound amino acids are in the region SIRIQRGPGRAFVT. Zvi *et al.* [1995a] (**antibody binding site definition and exposure**)
- 0.5beta: Type-specific neutralization of IIIB – does not neutralize SF2. Broder *et al.* [1994] (**variant cross-recognition or cross-neutralization**)
- 0.5beta: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro*. Cook *et al.* [1994] (**brain/CSF**)
- 0.5beta: Binding domain aa 310-319: RGPGRAFVTIGKIG – mutations in the V3 loop from basic residues can destroy virus infectivity and syncytium formation: R306T, R309T and R313G can also reduce binding of V3 MAbs with two different binding sites: 9284 and 0.5beta. Okada *et al.* [1994] (**antibody binding site definition and exposure**)
- 0.5beta: gp41 mutation that confers resistance to neutralization by anti-CD4 binding site antibodies does not reduce neutralizing efficiency of this V3 region MAb. Thali *et al.* [1994]
- 0.5beta: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to some antiserum and conformationally sensitive neutralizing MAbs – neutralization efficiency of 0.5beta is not affected. Klasse *et al.* [1993a]; Reitz *et al.* [1988] (**antibody binding site definition and exposure**)
- 0.5beta: Binding to native gp120 100-300 fold greater than to denatured. Moore *et al.* [1993b] (**antibody binding site definition and exposure**)
- 0.5beta: Monoclonal anti-idiotype antibodies that mimic the 0.5beta epitope were generated. Sperlagh *et al.* [1993] (**anti-idiotype**)
- 0.5beta: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – of the MAbs tested , 0.5beta neutralization was the most profoundly affected by this mutation. Watkins *et al.* [1993] (**escape**)
- 0.5beta: Neutralization of virus carrying an A to T substitution (contrast with MAb M77) di Marzo Veronese *et al.* [1993]
- 0.5beta: sCD4 causes loss of IIIB type-specificity, allowing binding and neutralization of MN, in contrast to MAb mu5.5. Maeda *et al.* [1992]
- 0.5beta: Chimeric mouse-human MAb Cbeta1 was constructed by combining the human Cgamma1 and Ckappa constant regions with the 0.5beta murine MAb – ADCC and neutralizing activity. Matsushita *et al.* [1992] (**complement**)

- 0.5beta: Potent neutralizing activity. D'Souza *et al.* [1991]
- 0.5beta: Emergence of virus resistant to MAb 0.5beta and autologous sera neutralization in IIIB infected chimps. Nara *et al.* [1990] (**escape**)
- 0.5beta: Type-specific neutralization of IIIB – does not neutralize MN or RF. Matsushita *et al.* [1988]; Skinner *et al.* [1988b] (**antibody generation**)

No. 544
MAb ID Cβ1, 0.5β
HXB2 Location gp160 (311–324)
Author Location gp120 (316–330 HXB2)
Epitope RGPGRAFVTIGKIG
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* Env
Species (Isotype) humanized mouse (IgG1)
Ab Type V3
References Ferrantelli & Ruprecht 2002; Kimura *et al.* 2002; Matsushita *et al.* 1992; Emini *et al.* 1992

- Cbeta1: Review of passive immunoprophylaxis with human NAbs that also includes this chimeric mouse-human MAb, noting it protected 2/2 Chimpanzees from HIV-1 IIIB infection in the Emini *et al.*study published in 1992. Ferrantelli & Ruprecht [2002]
- Cbeta1: Defines epitope as IQRGPGRA – strong neutralizing activity against NL4-3 (X4 virus) and none against JRFL (R5 virus) – used as a control in a study of NAb activity in patients undergoing HAART. Kimura *et al.* [2002]
- Cbeta1: passive transfer to chimpanzees confers protection against challenge with homologous cell-free virus – mouse 0.5beta human IgG1 chimera. Emini *et al.* [1992]
- Cbeta1: Chimeric mouse-human MAb Cbeta1 was constructed by combining the human Cgamma1 and Ckappa constant regions with the 0.5beta murine MAb – ADCC and neutralizing activity. Matsushita *et al.* [1992]

No. 545
MAb ID NM-01 (hNM01, hNM-01)
HXB2 Location gp160 (312–315)
Author Location gp120 (MN)
Epitope GPGR
Neutralizing L
Immunogen Vaccine
Vector/Type: human rhinovirus 14 *Strain:* B clade MN *HIV component:* V3
Species (Isotype) mouse (IgG)
Ab Type V3
Research Contact M. Terada, Jason Grabely
References Zwick *et al.* 2003; Nakamura *et al.* 2000; Smith *et al.* 1998; Yoshida *et al.* 1997; Ohno *et al.* 1991
Keywords antibody interactions, complement, immunotherapy

- NM-01: Called hNM01. scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. The humanized version of this MAb was one of the V3 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- NM-01: Called hNM01. The CDR region of the murine MAb NM-01 was put into a human IgG frame. The epitope recognition was preserved, but the neutralizing potency of the humanized form was enhanced. It could activate complement. Nakamura *et al.* [2000] (**complement**, **immunotherapy**)
- NM-01: The tip of the MN V3 loop was inserted into cold-causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and NM-01 was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN. Smith *et al.* [1998]
- NM-01: Resistance mutation selected by propagation of molecular cloned isolate in the presence of NM-01. Yoshida *et al.* [1997]

No. 546
MAb ID 1026
HXB2 Location gp160 (312–317)
Author Location gp120 (MN)
Epitope GPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp120
Species (Isotype) mouse (IgG)
Ab Type V3
References Bou-Habib *et al.* 1994; Nakamura *et al.* 1993

- 1026: Greater affinity for T cell-tropic strain T-CSF, derived from JR-CSF, than to the primary isolate JR-CSF. Bou-Habib *et al.* [1994]
- 1026: Bound diverse strains, neutralizing activity against MN, close to GPGRAF. Nakamura *et al.* [1993]

No. 547
MAb ID 1034
HXB2 Location gp160 (312–317)
Author Location gp120 (MN)
Epitope GPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp120
Species (Isotype) mouse (IgG)
Ab Type V3
References Berman *et al.* 1997; Bou-Habib *et al.* 1994

- 1034: Binds to 5/7 isolates from breakthrough cases from a MN gp120 vaccine trial. Berman *et al.* [1997]

- 1034: Greater affinity for T cell tropic T-CSF, derived from JR-CSF, than to the primary isolate JR-CSF, close to GPGRAF. Bou-Habib *et al.* [1994]

No. 548
MAb ID 59.1 (R/V3-59.1)
HXB2 Location gp160 (312–317)
Author Location gp120 (308–313 MN)
Epitope GPGRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN *HIV component:* V3
Species (Isotype) mouse (IgG1)
Ab Type V3
Research Contact Mary White-Scharf and A. Profy, Repligen Corporation
References York *et al.* 2001; Stanfield *et al.* 1999; Smith *et al.* 1998; Ghiara *et al.* 1997; Seligman *et al.* 1996; D'Souza *et al.* 1994; Bou-Habib *et al.* 1994; Ghiara *et al.* 1993; Potts *et al.* 1993; White-Scharf *et al.* 1993; D'Souza *et al.* 1991

- 59.1: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. York *et al.* [2001]
- 59.1: The crystal structure of V3 loop peptides bound to Fabs was obtained – conformational changes in the tip of the V3 loop (GPGR) were observed when different MAbs were bound. Stanfield *et al.* [1999]
- 59.1: The tip of the MN V3 loop was inserted into cold causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and 59.1 was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN. Smith *et al.* [1998]
- 59.1: A conformationally restricted analog of the tip of the V3 loop was constructed and bound with Fab 59.1 – crystal structure shows interactions between 59.1 and an MN peptide and 59.1 and the modified peptide are similar, but NMR studies reveal that the modified peptide is more ordered in solution, retaining the Fab bound form. Ghiara *et al.* [1997]
- 59.1: Competition ELISAs with serial deletions produced longer estimate of epitope length than x-ray crystallography or Alanine substitution, RIHIGPGRAFYTT, suggesting significance of non-contact residues. Seligman *et al.* [1996]
- 59.1: Greater affinity for T-cell tropic strain T-CSF than the primary isolate JR-CSF, from which T-CSF was derived. Bou-Habib *et al.* [1994]
- 59.1: Multi-lab study for antibody characterization and assay comparison – neutralizes MN and IIIB. D'Souza *et al.* [1994]
- 59.1: Crystal structure of a 24 amino acid peptide from the V3 loop bound to 59.1 Fab fragment – contact residues IGPGRAF. Ghiara *et al.* [1993]
- 59.1: Synergistic neutralization of MN when combined with sCD4 or the CD4BS MAb F105. Potts *et al.* [1993]
- 59.1: Epitope defined by peptide reactivity and binding affinity with amino acid substitutions – GPGRAF. White-Scharf *et al.* [1993]
- 59.1: Called R/V3-59.1 – potent neutralizing MAb. D'Souza *et al.* [1991]

No. 549
MAb ID polyclonal
HXB2 Location gp160 (312–317)
Author Location gp120 (316–321)
Epitope GPGRAF
Neutralizing
Immunogen Vaccine
Vector/Type: protein, polyepitope *HIV component:* gp160 *Adjuvant:* BSA
Species (Isotype) rabbit
Ab Type V3
References Lu *et al.* 2000b; Lu *et al.* 2000c

- High titer response to ELDKWA and RILAVERYLKD was observed upon vaccination with multiple-epitope vaccine CG-GPGRAFY-G-ELDKWA-G-RILAVERYLKD conjugated to BSA, a weak response to GPGRAFY – immunization with CG-(ELDKWA-GPGRAFY)_2-K was also tried, yielding a strong Ab response to ELDKWA, weak to GPGRAF – gp160 vaccination yielded strong Ab response but not to any of the peptides studied here. Lu *et al.* [2000c,b]

No. 550
MAb ID 10E3
HXB2 Location gp160 (312–318)
Author Location gp120 (317–323 IIIB)
Epitope GPGRAFY
Neutralizing
Immunogen Vaccine
Vector/Type: peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* B clade IIIB *HIV component:* V3
Species (Isotype) mouse (IgG)
Ab Type V3
References Li *et al.* 2002; Tian *et al.* 2001
Keywords vaccine antigen design

- 10E3: A polyepitope vaccine was designed based on a recombinant GST fusion protein containing three repeats of the 2F5 core epitope ELDKWA combined with the V3 region peptide GPGRAFY. Abs raised in mice could recognize the peptides, sgp41, and CHO-WT cells that expressed HIV-1 Env on their surface. Li *et al.* [2002] (**vaccine antigen design**)
- 10E3: Peptides GPGRAFY and ELDKWAG were conjugated to KLH and used to raise mouse monoclonal Ab – MAb hybridomas were generated with defined specificity – 10E3 binds to the peptide GPGRAFY and to rgp160. Tian *et al.* [2001]

No. 551
MAb ID polyclonal
HXB2 Location gp160 (312–318)
Author Location gp120 (317–323)
Epitope GPGRAFY
Neutralizing

Immunogen Vaccine
Vector/Type: peptide *HIV component:* V3
Adjuvant: BSA
Species (Isotype) rabbit, mouse
Ab Type V3
References Yu *et al.* 2000

- High levels of epitope-specific Abs were induced by the peptide-BSA conjugates C-(GPGRAF)_4-BSA or C-(TRPNNNTRKSIRIQRGPGRAFYTIG KI)-BSA but not by rgp160 vaccine. Yu *et al.* [2000]

No. 552
MAb ID N11-20 (110-H)
HXB2 Location gp160 (312–320)
Author Location gp120 (317–325)
Epitope GPGRAFVTI
Neutralizing L (LAI)
Immunogen
Species (Isotype) mouse (IgG1κ)
Ab Type V3
Research Contact J. C. Mazie, Hybridolab, Institut Pasteur
References Valenzuela *et al.* 1998

- N11-20: Neutralization of LAI in CEM cells by anti-V3 MAbs 110.4 and N11-20 is through inhibition of virus binding to the cell. Valenzuela *et al.* [1998]

No. 553
MAb ID 5025A (5025)
HXB2 Location gp160 (313–317)
Author Location gp120 (313–317 BH10)
Epitope pgRAF
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade BH10
HIV component: V3
Species (Isotype) mouse (IgG)
Ab Type V3
Research Contact Paul Durda, Du Pont de Nemours and Co
References D'Souza *et al.* 1991; Langedijk *et al.* 1991

- 5025: Called 5025 – strain specific weakly neutralizing. D'Souza *et al.* [1991]
- 5025A: Generation and fine mapping of murine MAbs. Langedijk *et al.* [1991]

No. 554
MAb ID N70-1.9b
HXB2 Location gp160 (313–318)
Author Location gp120 (316–322)
Epitope PGRAFY
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type V3
References Gorny & Zolla-Pazner 2004; Scott *et al.* 1990; Robinson *et al.* 1990a
Keywords ADCC, review, variant cross-recognition or cross-neutralization

- N70-1.9b: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- N70-1.9b: Type specificity. Robinson *et al.* [1990a] (**variant cross-recognition or cross-neutralization**)
- N70-1.9b: Type specific neutralization, ADCC directed against MN infected cells. Scott *et al.* [1990] (**ADCC**, **variant cross-recognition or cross-neutralization**)

No. 555
MAb ID 902
HXB2 Location gp160 (313–324)
Author Location gp120 (IIIB)
Epitope PGRAFVTIGKIG
Neutralizing L
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: gp160
Species (Isotype) mouse (IgG1κ)
Ab Type V3
Research Contact Bruce Chesebro, Rocky Mountain National Laboratory, Montana
References Ling *et al.* 2004; Sakaida *et al.* 1997; Earl *et al.* 1994; Broder *et al.* 1994; Laman *et al.* 1993; Chesebro & Wehrly 1988
Keywords antibody binding site definition and exposure

- 902: NIH AIDS Research and Reference Reagent Program: 522.
- 902: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of the V3 MAbs 694-98D and 447-52D, that both bind near the tip of the loop, was decreased by both thrombin and trypsin, 932 binding was only decreased by trypsin. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 902: V3-BH10 peptide with loop-structure inhibits IL-2 induced T-cell proliferation, thought to be due to altering intracellular signaling, and MAb 908 can block the peptide inhibition. Sakaida *et al.* [1997]
- 902: Epitope may be partially masked or altered in the oligomeric molecule. Broder *et al.* [1994]
- 902: Used as a control in a study of the influence of oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]
- 902: Strain specific neutralization of HIV. Chesebro & Wehrly [1988]

No. 556
MAb ID 694/98-D (694/98, 694.8, 694/98D)
HXB2 Location gp160 (314–317)
Author Location gp120 (IIIB)
Epitope GRAF
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)

Ab Type V3

Research Contact Dr. Zolla-Pazner, Veterans Affairs Center, NY, NY. zollas01@endeavor.med.nyu.edu

References Ling *et al.* 2004; Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Zwick *et al.* 2003; Zhang *et al.* 2002; He *et al.* 2002; Edwards *et al.* 2002; Park *et al.* 2000; Nyambi *et al.* 2000; Altmeyer *et al.* 1999; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Schonning *et al.* 1998; Nyambi *et al.* 1998; Andrus *et al.* 1998; Li *et al.* 1998; Smith *et al.* 1998; Zolla-Pazner *et al.* 1997; Li *et al.* 1997; Forthal *et al.* 1995; Zolla-Pazner *et al.* 1995; VanCott *et al.* 1995; Cook *et al.* 1994; VanCott *et al.* 1994; Laal *et al.* 1994; Gorny *et al.* 1994; Spear *et al.* 1993; Cavacini *et al.* 1993a; Gorny *et al.* 1993; Gorny *et al.* 1992; Gorny *et al.* 1991; Skinner *et al.* 1988b

Keywords antibody binding site definition and exposure, antibody interactions, review, variant cross-recognition or cross-neutralization

- 694/98D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 694/98-D: Called 694/98. V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using IIIB gp120. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 694-98D: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of the V3 MAbs 694-98D and 447-52D, that both bind near the tip of the loop, was decreased by both thrombin and trypsin. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 694/98D: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V3 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- 694/98-D: Called 694/98D – Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. Edwards *et al.* [2002]
- 694/98-D: Called 694 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. He *et al.* [2002]
- 694/98-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 694/98-D showed intermediate reactivity. Nyambi *et al.* [2000]
- 694/98-D: Called 694/98D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000]
- 694/98-D: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not linear V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies. Altmeyer *et al.* [1999]
- 694/98-D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a]
- 694/98-D: MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b]
- 694/98-D: Used to study pre- and post-exposure prophylaxis Hu-PBL-SCID mice infected by an intraperitoneal injection of HIV-1 LAI – MAb half-life in plasma in mice is 9 days – 2 hours post-694/98-D mice were challenged with LAI, and at an Ab concentration of 1.32 mg/Kg, 50% of the mice were infected – one of the infected mice carried the resistant form GRTF rather than GRAF (critical amino acids for binding are GRA) – post-exposure prophylaxis was effective if delivered 15 min post-exposure, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection. Andrus *et al.* [1998]
- 694/98-D: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontin-

uous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) Li *et al.* [1998]
- 694/98-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 694/98-D bound only to B and D clade virions and had limited cross reactivity. Nyambi *et al.* [1998]
- 694/98-D: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, anti-V3 MAbs were found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan more efficiently than HIV-BRU. Schonning *et al.* [1998]
- 694/98-D: The tip of the MN V3 loop was inserted into cold causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and 694/98-D was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN. Smith *et al.* [1998]
- 694/98-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – could only achieve 50% neutralization alone – all Ab combinations tested showed synergistic neutralization – 694/98-D has synergistic response with MAbs F105, 15e, b12, 2F5, 17b, 2G12, and 48d, and with HIVIG. Li *et al.* [1997]
- 694/98-D: ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995]
- 694/98-D: Human HIV-1 infected sera and MAb 694/98 have high reactivity to MN and RF infected H9 cells, but Genentech rec gp120 IIIB vaccine recipients do not. VanCott *et al.* [1995]
- 694/98-D: Serotyping study using flow-cytometry – bound GRAX bearing virus in 10/11 cases – somewhat conformation dependent. Zolla-Pazner *et al.* [1995]
- 694/98-D: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – V3 MAbs can inhibit gp120 binding to GalCer *in vitro* – binding of GalCer to gp120 inhibited but did not completely block MAb binding. Cook *et al.* [1994]
- 694/98-D: 50% neutralization of HIV-IIIB at a concentration of 0.15mug/ml. Gorny *et al.* [1994]
- 694/98-D: Potent neutralization of IIIB – no neutralization synergy in combination with CD4 binding domain MAbs. Laal *et al.* [1994]
- 694/98-D: GRVY did not alter peptide binding – GRVI and GQAW enhanced dissociation – GQVF and GQAL did not bind. VanCott *et al.* [1994]
- 694/98-D: Neutralizes MN and IIIB (GRAF) – binds SF2 (GRAF) – binding reactivity: MN, IIIB, SF2, NY5, RF, CDC4, WM52. Gorny *et al.* [1993]
- 694/98-D: Called 694-D – complement mediated virolysis of IIIB, but not in the presence of sCD4. Spear *et al.* [1993]
- 694/98-D: Type-specific lab isolate neutralization was observed – binds with 1-3 fold greater affinity to gp120 than to peptides. Gorny *et al.* [1992]
- 694/98-D: This MAb was first described here. Skinner *et al.* [1988b]

No. 557
MAb ID MO101/V3,C4
HXB2 Location gp160 (314–323)
Author Location gp120 (314–323)
Epitope GRAFVTIGKI+LGVAPTKAKR
Neutralizing
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
Ab Type V3-C4
References Ohlin *et al.* 1992
- MO101: Generated in response to IIIB Env 286-467 upon *in vitro* stimulation of uninfected-donor lymphocytes – reacts with peptides 314-323 + 494-503 from the V3 and C4 regions. Ohlin *et al.* [1992]

No. 558
MAb ID MO101/V3,C4
HXB2 Location gp160 (314–323)
Author Location gp120 (314–323)
Epitope GRAFVTIGKI+LGVAPTKAKR
Neutralizing
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
Ab Type V3-C5
References Ohlin *et al.* 1992
- MO101: Generated through *in vitro* stimulation of uninfected-donor lymphocytes with pB1 containing IIIB Env 286-467 – reacts with peptides from the V3 and C4 regions, positions 314-323 + 494-503, peptides GRAFVTIGKI + LGVAPTKAKR. Ohlin *et al.* [1992]

No. 559
MAb ID MO101/V3,C4
HXB2 Location gp160 (314–323)
Author Location gp120 (494–503)
Epitope GRAFVTIGKI+LGVAPTKAKR
Neutralizing
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
Ab Type V3-C5
References Ohlin *et al.* 1992
- MO101: Generated through *in vitro* stimulation of uninfected-donor lymphocytes with pB1 containing IIIB Env 286-467 – reacts with peptides from the V3 and C4 regions, positions 314-323 + 494-503, peptides GRAFVTIGKI + LGVAPTKAKR. Ohlin *et al.* [1992]

No. 560
MAb ID 9205 (NEA-9205 NEA9205)
HXB2 Location gp160 (315–317)
Author Location gp120 (IIIB)
Epitope RAF(corereactivity)
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: V3
Species (Isotype) mouse (IgG1)
Ab Type V3
Research Contact NEN, Boston MA, commercial
References Gram *et al.* 2002; Schonning *et al.* 1999; Schonning *et al.* 1998; Fontenot *et al.* 1995; VanCott *et al.* 1994; Allaway *et al.* 1993; Trujillo *et al.* 1993; Durda *et al.* 1990

- 9205: Also see MAb called 5023A.
- 9205: Called NEA9205 – gp120 capture ELISAs with MAbs D7324 (anti-C-term) or 9205 (anti-V3) were compared in a study of orientation of glycosylation sites – CD4 binding could only inhibit deglycosylation when gp120 was bound to the plate by D7324, not by 9205, while Abs from HIV-1 infected people inhibited deglycosylation most effectively when gp120 was caught by 9205. Gram *et al.* [2002]
- 9205: Called NEA-9205 – the stoichiometry of MAb neutralization was tested and the data indicated that binding for neutralization was was incremental not all or none, i.e., each envelope oligomer binds a single MAb and each Env oligomer bound reduces the chances of infection – 9205 binds only to Env with a glycosylation site mutation in the V3 loop, A308T. Schonning *et al.* [1999]
- 9205: Called NEA-9205 – The N306 glycan of the V3 loop makes the tip of the V3 loop inaccessible to this MAb in oligomeric Env, loss of this glycan enhances neutralization sensitivity. Schonning *et al.* [1998]
- 9205: Neutralizes IIIB but not MN – significantly slower dissociation constant for IIIB than MN. VanCott *et al.* [1994]
- 9205: Synergy with combinations of CD4-based molecules in inhibition of HIV-1 Env mediated cell fusion. Allaway *et al.* [1993]
- 9205: Called NEA-9205, epitope RIQRGPGRAFVTIGK – reacts with three human brain proteins of 35, 55, 110 kd molecular weight – similar to 9284 – RAF is the core reactivity. Trujillo *et al.* [1993]

No. 561
MAb ID 110.I
HXB2 Location gp160 (316–322)
Author Location gp120 (316–322)
Epitope AFVTIGK
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp120
Species (Isotype) mouse
Ab Type V3
Research Contact F. Traincard, Pasteur Institute, France
References Parren *et al.* 1998a; Wyatt *et al.* 1997; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; Moore *et al.* 1994c; Moore *et al.* 1993b

- 110.I: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- 110.I: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. Wyatt *et al.* [1997]
- 110.I: Reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – and enhances binding of some anti-V2 MAbs – binding enhanced by some anti-CD4 binding site MAbs. Moore & Sodroski [1996]
- 110.I: Epitope suggested to be RAFVTIGK – V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus, mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs. Poignard *et al.* [1996a]
- 110.I: Binds equally well to monomer and oligomer, rapid association and potent neutralization of lab strains. Sattentau & Moore [1995]
- 110.I: Binds to carboxy-terminal side of the V3 loop – inhibits binding of C4 region MAb G3-299. Moore *et al.* [1993b]

No. 562
MAb ID anti-HIV-2 polyclonal
HXB2 Location gp160 (317–320)
Author Location gp120 (315–318 SBL6669 HIV-2)
Epitope FHSQ+WCR
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* HIV-2 SBL6669-ISY *HIV component:* V3
Species (Isotype) guinea pig (IgG)
Ab Type V3
References Morner *et al.* 1999

- Neutralizing Abs against HIV-2 V3 are produced when peptides spanning two non-contiguous parts of the V3 loop are used for vaccination including amino acids 315-318 near the tip (FHSQ) and 329-331 (WCR) at the C-term Cys. Morner *et al.* [1999]

No. 563
MAb ID IIIB-V3-01
HXB2 Location gp160 (320–328)
Author Location gp120 (IIIB)
Epitope IGKIGNMRQ
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *HIV component:* V3
Species (Isotype) mouse (IgG1)
Ab Type V3
Research Contact Jon Laman
References Laman *et al.* 1993

- IIIB-V3-01: UK Medical Research Council AIDS reagent: ARP3046.
- IIIB-V3-01: NIH AIDS Research and Reference Reagent Program: 1726.
- IIIB-V3-01: Specific for carboxy-terminal flank of the IIIB V3 loop – epitope is hidden native gp120, exposed on denaturation. Laman *et al.* [1993]

No. 564
MAb ID D/6D1
HXB2 Location gp160 (346–377)
Author Location gp120 (351–382 LAI)
Epitope ASKLREQFGNNKTIIFKQSSGGDPEIVTHSFN
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp120

Species (Isotype) mouse (IgG1)
Ab Type V4
References Bristow *et al.* 1994

- D/6D1: V4 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. Bristow *et al.* [1994]

No. 565
MAb ID 4D7/4
HXB2 Location gp160 (360–380)
Author Location gp120 (361–380 LAI)
Epitope IFKQSSGGDPEIVTHSFNCGG
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: Env
Species (Isotype) mouse (IgG)
Ab Type V4
Research Contact S. Ranjbar, NIBSC, UK
References Moore *et al.* 1994c

- 4D7/4: UK Medical Research Council AIDS reagent: ARP3051.
- 4D7/4: C3 region – the relative affinity for denatured/native gp120 is >10. Moore *et al.* [1994c]

No. 566
MAb ID 36.1(ARP 329)
HXB2 Location gp160 (361–381)
Author Location gp120 (362–381 LAI)
Epitope FKQSSGGDPEIVTHSFNCGGE
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: Env
Species (Isotype) mouse (IgG)
Ab Type V4
References Moore *et al.* 1994c; Thiriart *et al.* 1989

- 36.1: UK Medical Research Council AIDS reagent: ARP329.
- 36.1: The relative affinity for denatured/native gp120 is >30 – mutations 380 G/F, 381 E/P impair binding. Moore *et al.* [1994c]

No. 567
MAb ID C12
HXB2 Location gp160 (361–381)
Author Location gp120 (362–381 LAI)
Epitope FKQSSGGDPEIVTHSFNCGGE
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
Ab Type V4
Research Contact George Lewis
References Moore *et al.* 1994d; Abacioglu *et al.* 1994; Moore *et al.* 1994c; Moore & Ho 1993

- C12: C3 region – epitope boundaries mapped by peptide scanning, core FNCGG. Abacioglu *et al.* [1994]
- C12: The relative affinity for denatured/native gp120 is >30 – mutations 380 G/F, 381 E/P, and 384 Y/E impair binding – also binds GEFFYCNSTQLFNS, gp120(380-393 LAI) Moore *et al.* [1994c]
- C12: Bound preferentially to denatured IIIB gp120. Moore & Ho [1993]

No. 568
MAb ID 110.D
HXB2 Location gp160 (380–393)
Author Location gp120 (380–393 LAI)
Epitope GEFFYCNSTQLFNS
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: Env
Species (Isotype) mouse (IgG)
Ab Type C3
Research Contact F. Traincard, Pasteur Institute, France
References Valenzuela *et al.* 1998; Moore *et al.* 1994c

- 110.D: The relative affinity for denatured/native gp120 is >50. Moore *et al.* [1994c]

No. 569
MAb ID B32
HXB2 Location gp160 (380–393)
Author Location gp120 (380–393 LAI)
Epitope GEFFYCNSTQLFNS
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
Ab Type C3
References Abacioglu *et al.* 1994; Moore *et al.* 1994c

- B32: C3 region – epitope boundaries mapped by peptide scanning – FFY(core) Abacioglu *et al.* [1994]
- B32: The relative affinity for denatured/native gp120 is >100 – mutations 380 G/F, 381 G/P, 382 F/L, 384 Y/E, and 386 N/R impair binding. Moore *et al.* [1994c]

No. 570
MAb ID polyclonal (VEI4)
HXB2 Location gp160 (391–413)
Author Location Env
Epitope FNSTWFNSTWSTEGSNNTEGSDT
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V4
References Carlos *et al.* 1999

- Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGP-GRAFYTTGDIGNIRQ. Carlos *et al.* [1999]

No. 571
MAb ID B15
HXB2 Location gp160 (395–400)
Author Location gp120 (395–400 BH10)
Epitope WFNSTW
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG2b)
Ab Type V4
Research Contact George Lewis
References Abacioglu *et al.* 1994; Moore *et al.* 1993b; Moore & Ho 1993

- B15: V4 region – epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]
- B15: Bound preferentially to denatured IIIB gp120. Moore & Ho [1993]
- B15: Binds native BH10 gp120 with 5 fold less affinity than denatured – does not bind native or denatured MN gp120. Moore *et al.* [1993b]

No. 572
MAb ID B34
HXB2 Location gp160 (395–400)
Author Location gp120 (395–400 BH10)
Epitope WFNSTW
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG2b)
Ab Type V4
References Abacioglu *et al.* 1994

- B34: V4 region – epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 573
MAb ID E51
HXB2 Location gp160 (420–423)
Author Location gp120 (420–423 HXB2)
Epitope IKQI
Subtype B
Neutralizing P
Immunogen
Species (Isotype) human
Ab Type CD4i
Research Contact Joseph Sodroski, joseph_sodroski@dfci.harvard.edu
References Xiang *et al.* 2003
Keywords antibody binding site definition and exposure, antibody generation, co-receptor, inter-clade comparisons, variant cross-recognition or cross-neutralization

- E51: E51 recognizes a highly conserved epitope localized in the basic β19-strand (gp120 aa420-423), a region involved in CCR5 binding. The MAb was isolated from a EBV transformed B-cell line established from an HIV+ individual undergoing early STI. Fab fragments were also produced. E51, like CD4i MAb 17b, blocks CCR5 binding to sCD4-bound gp120. The presence of sCD4 induces a conformational change in gp120, which enhances ligand recognition. The substitutions E381R, F383S, R419D I420R, K421D, Q422L, I423S, and Y435S (HXB2 numbering) all severely reduce 17b and E51 binding. All but I423S also diminish CCR5 binding by more than 50%. The mutation F383S also inhibits sCD4 binding and CD4BS MAb F105 binding, and K421D inhibits F105 binding, but not sCD4. E51 has more cross-neutralizing potency than other prototype CD4i MAbs (17b) for B and C clade isolates. E51 and 17b both neutralized HIV-1 clade B strains HXBc2 and ADA, while JR-FL and 89.6 were only neutralized by E51, not 17b. Clade C strains MCGP1.3 and SA32 were both inhibited by 17b and E51, but E51 was more potent against SA32. Xiang *et al.* [2003] (**antibody binding site definition and exposure**, **antibody generation**, **co-receptor**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 574
MAb ID JL413
HXB2 Location gp160 (421–436)
Author Location gp160 (421–436)
Epitope KQIINMWQEVGKAMYA
Subtype B
Neutralizing P
Immunogen autoimmune disease
Species (Isotype) human
Ab Type CD4BS
References Karle *et al.* 2004
Keywords antibody generation, antibody sequence, variable domain, co-receptor, inter-clade comparisons

- JL413: Phage display was used to create a library of gp120-binding single-chain fragments containing V domain (scFv) constructs derived from PBMC of lupus patients. Lupus patients rarely get HIV/AIDS and can make antibodies that bind to a conserved gp120 determinant. The scFV clone JL413 was able to induce dose-dependent, cross-clade neutralization of primary HIV-1 isolates ZA009 (R5, clade C); BR004 (R5, clade C); Ug046 (X4, clade D); SF162 (R5, clade B), and 231135 (clade B). The scFV clone JL413 recognizes a linear region that overlaps the CD4 T-cell binding site, in contrast to HIV-induced MAbs that bind to this region and are conformation dependent. Karle *et al.* [2004] (**antibody generation**, **co-receptor**, **inter-clade comparisons**, **antibody sequence, variable domain**)

No. 575
MAb ID 5C2E5
HXB2 Location gp160 (422–431)
Author Location gp120 (406–415 IIIB)

Epitope QFINMWQEVK
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp120
Species (Isotype) mouse
Ab Type C4
Research Contact T. Gregory and R. Ward, Genentech, San Francisco
References Cordell *et al.* 1991; Lasky *et al.* 1987

- 5C2E5: Cross-competition with MAbs 5C2E5, ICR38.8f and ICR38.1a. Cordell *et al.* [1991]
- 5C2E5: Blocks the gp120-CD4 interaction. Lasky *et al.* [1987]

No. 576
MAb ID G3-211
HXB2 Location gp160 (423–437)
Author Location gp120 (423–437 IIIB)
Epitope IINMWQKVGKAMYAP
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C4
References Sun *et al.* 1989

- G3-211, 42, 299, 508, 519, 536, 537: Cross-react with diverse strains by immunofluorescence – blocks HIV binding to CD4+ cells – different neutralization efficiencies. Sun *et al.* [1989]

No. 577
MAb ID G3-537
HXB2 Location gp160 (423–437)
Author Location gp120 (423–437 IIIB)
Epitope IINMWQKVGKAMYAP
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C4
References Zwick *et al.* 2003; McKeating *et al.* 1992b; Ho *et al.* 1991b; Sun *et al.* 1989
Keywords antibody interactions

- G3-537: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the C4 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- G3-537: Weakly neutralizing – binds to a linear binding domain of gp120, NMWQEVGKAMYAPPISG. McKeating *et al.* [1992b]
- G3-537, 211, 299, 508, 519, 536, 42: Cross-react with diverse strains by immunofluorescence – blocks HIV binding to CD4+ cells – different neutralization efficiencies. Sun *et al.* [1989]

No. 578
MAb ID polyclonal
HXB2 Location gp160 (425–436)
Author Location gp120
Epitope NMWQEVGKAMYA
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB *Adjuvant:* Cholera toxin (CT)
Species (Isotype) mouse (IgA)
Ab Type CD4BS
References Bukawa *et al.* 1995

- Polyclonal secretory IgA antibody raised by mucosal immunization is able to neutralize IIIB, SF2, and MN – HIV-1 neutralization may be due to the V3, CD4 or HPG30 component of the multicomponent peptide immunogen. Bukawa *et al.* [1995]

No. 579
MAb ID 1795
HXB2 Location gp160 (425–441)
Author Location gp120 (425–441 IIIB)
Epitope NMWQEVGKAMYAPPISG
Neutralizing L
Immunogen Vaccine
Vector/Type: poliovirus *HIV component:* Env
Species (Isotype)
Ab Type CD4BS
References McKeating *et al.* 1992b

- 1795: CD4 binding site – weakly neutralizing – binding inhibited by WQEVGKAMYA, GKAM may be involved. McKeating *et al.* [1992b]

No. 580
MAb ID ICR38.1a (38.1a, 388/389, ARP388/389)
HXB2 Location gp160 (429–438)
Author Location gp120 (427–436 BRU)
Epitope EVGKAMYAPP
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10 *HIV component:* gp120
Species (Isotype) rat (IgG2b)
Ab Type C3, C4
References Vella *et al.* 2002; Kropelin *et al.* 1998; Peet *et al.* 1998; Jeffs *et al.* 1996; Moore *et al.* 1993b; McKeating *et al.* 1993a; McKeating *et al.* 1993b; McKeating *et al.* 1992c; McKeating *et al.* 1992a; McKeating *et al.* 1992b; Cordell *et al.* 1991

- ICR38.1a: UK Medical Research Council AIDS reagent: ARP388/ARP389.

- ICR38.1a: Called ARP388/ARP389: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs – lists epitope as WQEVGKAMYA. Vella *et al.* [2002]
- ICR38.1a: Called 388/389 – anti-C1 region MAb 87-135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) Kropelin *et al.* [1998]
- ICR38.1a: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – ICR38.1a was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]
- ICR38.1a: Called 38.1a – 10 to 20 fold increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. Jeffs *et al.* [1996]
- ICR38.1a: Studied in the context of a neutralization escape mutant. McKeating *et al.* [1993a]
- ICR38.1a: Unreactive with solid-phase decapeptide, competed in solution phase assay – ICR 38.1a and ICR 38.8f were initially reported to be independent MAbs, but are actually subclones of the same MAb. Moore *et al.* [1993b]
- ICR38.1a: Weakly neutralizing – binds linear determinant in the CD4 binding domain – cross-competition with MAbs G3-536, 5C2E5, and ICR38.8f. Cordell *et al.* [1991]; McKeating *et al.* [1992b]
- ICR38.1a: Unable to exert a synergistic effect in combination with V3 directed MAbs, in contrast to MAb 39.13g, that binds to a conformational epitope involved in CD4 binding. McKeating *et al.* [1992a]

No. 581
MAb ID G3-299
HXB2 Location gp160 (429–438)
Author Location gp120 (429–438 BRU)
Epitope EVGKAMYAPP
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C4
Research Contact M. Fung and Tanox Biosystems Inc and David Ho, ADARC, NY
References Zwick *et al.* 2003; Kwong *et al.* 2002; Parren *et al.* 1998a; Wyatt *et al.* 1997; Ditzel *et al.* 1997; Binley *et al.* 1997a; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; Moore *et al.* 1993b; Sun *et al.* 1989
Keywords antibody binding site definition and exposure, antibody interactions

- G3-299: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the C4-V3 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- G3-299: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the G3-299 epitope as V3 loop/outer domain. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- G3-299: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- G3-299: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. Wyatt *et al.* [1997]
- G3-299: Discontinuous V3-C4 epitope, binding enhanced by a few anti-C1, anti-CD4 binding site, and V2 MAbs – binding reciprocally inhibited by anti-V3 MAbs – G3-229 enhances the binding of some anti-V2 MAbs. Moore & Sodroski [1996]
- G3-299: Epitope described as KQIINMWQKVGKAMYAPPIS – binding resulted in slight gp120 dissociation from virus and exposure of the gp41 epitope for MAb 50-69. Poignard *et al.* [1996a]
- G3-299: Binds with higher affinity to monomer than to oligomer, slow association rate, although faster than other C4 MAbs tested, with more potent neutralization of lab strain. Sattentau & Moore [1995]
- G3-299: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – G3-42, G3-299 lower affinity than G3-508, G3-519, and G3-536 – bound native gp120, not denatured – poor peptide binding,

epitope spans V3-C4 regions – 433A/L, 435Y/H and 430V/S substitutions impaired binding, V3 loop cleavage or insertion abolished binding. Moore *et al.* [1993b]
- G3-299: Best neutralization of IIIB in panel of 7 MAbs that bind overlapping epitope. Sun *et al.* [1989]

No. 582
MAb ID G3-42 (G3 42)
HXB2 Location gp160 (429–438)
Author Location gp120 (429–438 BRU)
Epitope EVGKAMYAPP
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C4
Research Contact Tanox Biosystems Inc and David Ho, ADARC, NY
References Zwick *et al.* 2003; Jagodzinski & Trzeciak 2000; Binley *et al.* 1999; Binley *et al.* 1997a; Trkola *et al.* 1996a; Poignard *et al.* 1996a; Moore & Sodroski 1996; Jagodzinski *et al.* 1996; Sattentau & Moore 1995; Thali *et al.* 1993; Moore *et al.* 1993b; Sun *et al.* 1989
Keywords antibody interactions

- G3-42: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the C4-V3 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- 0.5beta: MAbs 0.5beta and G3-42 were used to study synthesis of oligomeric and monomeric forms of Env – inhibition of glycosylation by tunicamycin results in reduction of oligomeric gp120 at the cell surface and of monomer in the cytoplasm – neither MAb recognized non-glycosylated Env precursor. Jagodzinski & Trzeciak [2000]
- G3-42: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999]
- G3-42: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS potently inhibits G3-42 binding – G3-42 epitope described as KVGKAMYAPP. Jagodzinski *et al.* [1996]
- G3-42: Inhibits binding of many anti-V3, -CD4 binding site, and -C4 region MAbs – enhances binding of some anti-V2 region MAbs. Moore & Sodroski [1996]
- G3-42: Epitope described as KQIINMWQKVGKAMYAPPIS – binding resulted in slight gp120 dissociation from virus and exposure of the gp41 epitope for MAb 50-69. Poignard *et al.* [1996a]
- G3-42: Called G3 42 – Does not inhibit gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study – described as V3-C4 discontinuous epitope. Trkola *et al.* [1996a]
- G3-42: Binds with higher affinity to monomer than to oligomer, slow association rate. Sattentau & Moore [1995]
- G3-42: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – G3-42, G3-299 have lower affinity than G3-508, G3-519, and G3-536 – bound native gp120, not denatured – poor peptide binding, epitope spans V3-C4 regions – 433A/L, 435Y/H and 430V/S substitutions impaired binding, V3 loop insertion abolished binding. Moore *et al.* [1993b]
- G3-42: Inhibits binding of CD4 inducible MAb 48d. Thali *et al.* [1993]
- G3-42: Neutralization of IIIB but not RF. Sun *et al.* [1989]

No. 583
MAb ID G3-508 (G3 508)
HXB2 Location gp160 (429–438)
Author Location gp120 (429–438 BRU)
Epitope EVGKAMYAPP
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C4
Research Contact M. Fung and Tanox Biosystems Inc and David Ho, ADARC, NY
References Binley *et al.* 1998; Parren *et al.* 1998a; Binley *et al.* 1997a; Trkola *et al.* 1996a; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; Moore *et al.* 1993b; Thali *et al.* 1993; Sun *et al.* 1989

- G3-508: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- G3-508: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]

- G3-508: Inhibits binding of some V3, C4 and CD4 binding site MAbs, enhances binding of V2 region MAbs. Moore & Sodroski [1996]
- G3-508: Binding resulted in slight gp120 dissociation from virus and exposure of the gp41 epitope for MAb 50-69. Poignard *et al.* [1996a]
- G3-508: Called G3 508 – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]
- G3-508: Binds with higher affinity to monomer than to oligomer, slow association rate. Sattentau & Moore [1995]
- G3-508: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – bound denatured with 10 fold greater affinity than native – 433A/L, 435Y/H and 430V/S substitutions impaired binding. Moore *et al.* [1993b]
- G3-508: Inhibits binding of CD4 inducible MAb 48d. Thali *et al.* [1993]
- G3-508: Neutralization of IIIB and RF. Sun *et al.* [1989]

No. 584
MAb ID G3-519
HXB2 Location gp160 (429–438)
Author Location gp120 (429–438 BRU)
Epitope EVGKAMYAPP
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C4
Research Contact Tanox Biosystems Inc and David Ho, ADARC, NY
References Zwick *et al.* 2003; Binley *et al.* 1999; Parren *et al.* 1998a; Wyatt *et al.* 1997; Binley *et al.* 1997a; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; D'Souza *et al.* 1994; Moore *et al.* 1993b; Moore & Ho 1993; Sun *et al.* 1989
Keywords antibody interactions

- G3-519: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the C4 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- G3-519: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999]
- G3-519: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- G3-519: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. Wyatt *et al.* [1997]
- G3-519: Non-reciprocal enhanced binding in the presence of the C5 MAb 1C1 and the C1 MAb 135/9 – reciprocal enhanced binding with some V2 MAbs. Inhibited binding the presence of some C4, V3 and CD4 binding site MAbs. Moore & Sodroski [1996]
- G3-519: Epitope described as KVGKAMYAPP – binding resulted in slight gp120 dissociation from virus but no significant exposure of the gp41 epitope for MAb 50-69. Poignard *et al.* [1996a]
- G3-519: Binds with higher affinity to monomer than to oligomer, slow association rate. Sattentau & Moore [1995]
- G3-519: Included in a multi-lab study for antibody characterization, and binding and neutralization assay comparison, also binds IIIB: IINMWQKVGKAMYAPP. D'Souza *et al.* [1994]
- G3-519: Neutralizes IIIB, is reactive with SF-2 gp120, mild inhibition of HIV-1 + sera binding to IIIB gp120. Moore & Ho [1993]
- G3-519: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – bound denatured with 5 fold greater affinity than native – 433A/L, 435Y/H, 438P/R and 430V/S substitutions impaired binding. Moore *et al.* [1993b]
- G3-519: Best neutralization of RF in panel of 7 MAbs that bind overlapping epitope. Sun *et al.* [1989]

No. 585
MAb ID G3-536
HXB2 Location gp160 (429–438)
Author Location gp120 (429–438 BRU)
Epitope EVGKAMYAPP
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C4
Research Contact Tanox Biosystems Inc and David Ho, ADARC, NY
References Parren *et al.* 1998a; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; Gorny *et al.* 1994; Moore *et al.* 1993b; Moore & Ho 1993; McKeating *et al.* 1992b;

Cordell *et al.* 1991; Ho *et al.* 1991b; Sun *et al.* 1989

- G3-536: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- G3-536: Inhibits binding of some V3, C4 and CD4 binding site MAbs, enhances binding of V2 region MAbs. Moore & Sodroski [1996]
- G3-536: Epitope described as KVGKAMYAPP. Poignard *et al.* [1996a]
- G3-536: Binds with higher affinity to monomer than to oligomer, slow association rate. Sattentau & Moore [1995]
- G3-536: Enhances binding of anti-V2 MAb 697-D. Gorny *et al.* [1994]
- G3-536: Neutralizes IIIB, is reactive with SF-2 gp120, mild inhibition of HIV-1 + sera binding to IIIB gp120. Moore & Ho [1993]
- G3-536: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – bound denatured with 15 fold greater affinity than native – 433A/L, 435Y/H, 438P/R, and 430V/S substitutions impaired binding. Moore *et al.* [1993b]
- G3-536: Weakly neutralizing – binds to a linear determinant in the CD4 binding domain of gp120. McKeating *et al.* [1992b]
- G3-536: Cross-competition with MAbs 5C2E5, ICR38.8f and ICR38.1a. Cordell *et al.* [1991]
- G3-536: Weak neutralization of IIIB and RF – cross-react with diverse strains by immunofluorescence – blocks HIV binding to CD4+ cells – epitope:IINMWQKVGKAMYAP. Sun *et al.* [1989]

No. 586
MAb ID ICR38.8f
HXB2 Location gp160 (429–438)
Author Location gp120 (429–438 BRU)
Epitope EVGKAMYAPP
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10 *HIV component:* gp120
Species (Isotype) rat (IgG2b)
Ab Type C4
References Moore *et al.* 1993b; Cordell *et al.* 1991

- ICR38.8f:ICR 38.1a and ICR 38.8f were initially reported to be independent MAbs, but are actually subclones of the same MAb. Moore *et al.* [1993b]
- ICR38.8f: Weakly neutralizing – binds linear determinant in the CD4 binding domain – cross-competition with ICR38.1a, 5C2E5, and G3-536. Cordell *et al.* [1991]

No. 587
MAb ID MO86/C3
HXB2 Location gp160 (429–443)
Author Location gp120 (429–443)
Epitope EVGKAMYAPPISGQI
Neutralizing
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
Ab Type C4
References Ohlin *et al.* 1992

- MO86: Generated in response to IIIB Env 286-467 upon *in vitro* stimulation of uninfected-donor lymphocytes. Ohlin *et al.* [1992]

No. 588
MAb ID 13H8
HXB2 Location gp160 (431–440)
Author Location gp120 (412–453)
Epitope GKAMYAPPIS
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN
Species (Isotype) mouse (IgG)
Ab Type C4
References Jeffs *et al.* 1996; Nakamura *et al.* 1993; Nakamura *et al.* 1992

- 13H8: Binds V3 and C4 peptides (J. P. Moore, per. comm.)
- 13H8: 3 and 4.5 fold increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120, respectively. Jeffs *et al.* [1996]
- 13H8: Bound diverse strains, neutralizing activity against MN. Nakamura *et al.* [1993]
- 13H8: Cross blocks 5C2 in IIIB-rsgp160 ELISA – reactive with diverse strains in rgp120 ELISA. Nakamura *et al.* [1992]

No. 589
MAb ID G45-60
HXB2 Location gp160 (431–440)
Author Location gp120 (429–438 BRU)
Epitope GKAMYAPPIS
Neutralizing L
Immunogen Vaccine
Vector/Type: virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type C4
References Jagodzinski *et al.* 1996; Moore & Sodroski 1996; Gorny *et al.* 1994; Moore *et al.* 1993b; Sun *et al.* 1989

- G45-60: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus CRDS inhibits G45-60 binding. Jagodzinski *et al.* [1996]
- G45-60: Non-reciprocal enhancement of G45-60 binding by some C1 and C5 antibodies – reciprocal enhancement of some V2 region MAbs – reciprocal inhibition with many MAbs that bind to the V3, C4 and CD4 binding site regions. Moore & Sodroski [1996]
- G45-60: Enhances binding of anti-V2 MAb 697-D. Gorny *et al.* [1994]
- G45-60: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPI, decapeptide flanking peptides also bound – bound equivalently to native and denatured gp120 – 433A/L and 435Y/H (not 430V/S) substitutions impaired binding. Moore *et al.* [1993b]

No. 590
MAb ID polyclonal
HXB2 Location gp160 (432–451)

Author Location gp120 (42–61 LAI)
Epitope KAMYAPPISGQIRCSSNITG
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *HIV component:* Env
Species (Isotype) mouse
Ab Type C4
References Collado *et al.* 2000

- Vaccinia p14 can elicit NAbs and p39 tends to be immunodominant, so these two proteins were fused to regions of HIV-1 Env – reduced glycosylation was noted when p14 or p39 was placed in the N-term region of the fusion protein – chimeric proteins shifted the Env Ab response from V3 to either a C1 or C4 domain, depending on the construct – all chimeric Env proteins: 14kEnv, 39kEnv, and Env39k elicited a strong Ab response to the C1 region of gp120 (LFCASDAKAYDTEVHNVWAT), and Env39k mounted a strong response to the C4 region (KAMYAPPISGQIRCSSNITG) Collado *et al.* [2000]

No. 591
MAb ID 1662
HXB2 Location gp160 (433–439)
Author Location gp120 (IIIB)
Epitope AMYAPPI
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *HIV component:* Env
Species (Isotype)
Ab Type C4
References McKeating *et al.* 1992b

- 1662: Did not bind to native gp120, epitope not exposed. McKeating *et al.* [1992b]

No. 592
MAb ID 1663
HXB2 Location gp160 (433–439)
Author Location gp120 (IIIB)
Epitope AMYAPPI
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *HIV component:* Env
Species (Isotype)
Ab Type C4
References McKeating *et al.* 1992b

- 1663: Did not bind to native gp120, epitope not exposed. McKeating *et al.* [1992b]

No. 593
MAb ID 1664
HXB2 Location gp160 (433–439)
Author Location gp120 (IIIB)
Epitope AMYAPPI
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *HIV component:* Env
Species (Isotype)
Ab Type C4
References McKeating *et al.* 1992b

- 1664: Did not bind to native gp120, epitope not exposed. McKeating *et al.* [1992b]

No. 594
MAb ID 1697
HXB2 Location gp160 (433–439)
Author Location gp120 (IIIB)
Epitope AMYAPPI
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *HIV component:* Env
Species (Isotype)
Ab Type C4
References McKeating *et al.* 1992b

- 1697: Did not bind to native gp120, epitope not exposed. McKeating *et al.* [1992b]

No. 595
MAb ID 1794
HXB2 Location gp160 (433–442)
Author Location gp120 (IIIB)
Epitope AMYAPPISGQ
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *HIV component:* Env
Species (Isotype)
Ab Type C4
References McKeating *et al.* 1992b

- 1794: Did not bind to native gp120, epitope not exposed. McKeating *et al.* [1992b]

No. 596
MAb ID 1804
HXB2 Location gp160 (433–442)
Author Location gp120 (IIIB)
Epitope AMYAPPISGQ
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *HIV component:* Env
Species (Isotype)
Ab Type C4
References McKeating *et al.* 1992b

- 1804: Did not bind to native gp120, epitope not exposed. McKeating *et al.* [1992b]

No. 597
MAb ID 1807
HXB2 Location gp160 (433–442)
Author Location gp120 (IIIB)
Epitope AMYAPPISGQ
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *HIV component:* Env
Species (Isotype)

Ab Type C4
References McKeating *et al.* 1992b

- 1807: Did not bind to native gp120, epitope not exposed. McKeating *et al.* [1992b]

No. 598
MAb ID 1808
HXB2 Location gp160 (433–442)
Author Location gp120 (IIIB)
Epitope AMYAPPISGQ
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *HIV component:* Env
Species (Isotype)
Ab Type C4
References McKeating *et al.* 1992b

- 1808: Did not bind to native gp120, epitope not exposed. McKeating *et al.* [1992b]

No. 599
MAb ID polyclonal (VEI5)
HXB2 Location gp160 (454–474)
Author Location Env
Epitope LTRDGGNNNNESEIFRPGGGD
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V1, V2, V3, V4, V5
References Carlos *et al.* 1999

- Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ. Carlos *et al.* [1999]

No. 600
MAb ID polyclonal
HXB2 Location gp160 (460–467)
Author Location gp120 (LAI)
Epitope NNNNGSEI
Subtype B
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* gp160
Species (Isotype) human
Ab Type V5
References Loomis-Price *et al.* 1997

- HIV-1 + positive individuals were given a gp160 vaccine as immunotherapy, and this region was the most reactive new epitope as measured by a modified Pepscan technique which improved sensitivity – 4/14 showed vaccine-induced reactivity. Loomis-Price *et al.* [1997]

No. 601
MAb ID CRA1(ARP 323) (CRA-1)
HXB2 Location gp160 (461–470)
Author Location gp120 (451–470 LAI)
Epitope SNNESEIFRL
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type V5-C5
Research Contact M. Page, NIBSC, UK
References Yang *et al.* 2000; Trkola *et al.* 1996a; Moore & Sodroski 1996; Moore *et al.* 1994c; Moore *et al.* 1994d; Moore & Ho 1993

- CRA1: UK Medical Research Council AIDS reagent: ARP323.
- CRA1: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000]
- CRA1: C5 region linear epitope, binds weakly to nondenatured monomeric gp120 – reciprocal binding inhibition with anti-C5 antibodies 1C1 and M91 – non-reciprocal binding enhancement some C1 and V2 antibodies – non-reciprocal binding inhibition of some CD4 binding site antibodies. Moore & Sodroski [1996]
- CRA1: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]
- CRA1: Some C5 mutations abrogate binding 470 P/L or G, 475 M/S, some C2 mutations enhance binding. Moore *et al.* [1994d]
- CRA1: The relative affinity for denatured/native gp120 is 24 – C5 mutations 470 P/L or G, 475 M/S impairs binding to the native gp120 – only mutation 470 P/L impairs binding to denatured. Moore *et al.* [1994c]
- CRA1: Bound preferentially to denatured IIIB and SF2 gp120. Moore & Ho [1993]

No. 602
MAb ID M91
HXB2 Location gp160 (461–470)
Author Location gp120 (451–470 LAI)
Epitope SNNESEIFRL
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) rat (IgG2a)
Ab Type V5-C5
Research Contact Fulvia di Marzo Veronese
References Zwick *et al.* 2003; Yang *et al.* 2000; Binley *et al.* 1998; Ditzel *et al.* 1997; Moore & Sodroski 1996; Moore *et al.* 1994d; Moore *et al.* 1994c; di Marzo Veronese *et al.* 1992

Keywords antibody interactions

- M91: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding MAb that had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)
- M91: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000]
- M91: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- M91: C5 region linear epitope, binds weakly to nondenatured monomeric gp120 – M91 binding was enhanced by 1C1, but 1C1 binding was inhibited by M91 – non-reciprocal binding enhancement of C1 and V2 antibodies – non-reciprocal binding inhibition of CD4 binding site antibodies. Moore & Sodroski [1996]
- M91: The relative affinity for denatured/native gp120 is 24 – mutation in position 470 P/L impairs binding. Moore *et al.* [1994c]
- M91: 470 P/L impairs binding, but not 475 D/V, in contrast to CRA1 – some C2 mutations can enhance binding. Moore *et al.* [1994d]
- M91: Immunoblot reactive, RIP negative, but precipitates deglycosylated gp120 – reacts with strains IIIB, 451, MN, RF, and RUTZ. di Marzo Veronese *et al.* [1992]

No. 603
MAb ID 9201
HXB2 Location gp160 (471–482)
Author Location gp120 (475–486 LAI)
Epitope GGGDMRDNWRSE
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide
Species (Isotype) mouse (IgG1)
Ab Type C5
Research Contact Du Pont de Nemours, Boston, MA
References Dairou *et al.* 2004; McDougal *et al.* 1996
Keywords antibody binding site definition and exposure

- 9201: This paper describes a slightly different epitope, stating 9201 was raised against the peptide MRDNWRSELIKY, located within the alpha 5 helix in the C5 terminal region of gp120. Two MAbs were used to determine the photodamage location in HIV-1 Env induced by sulfonated anionic porphyrins. The negatively charged porphyrins interact with positive charge in the V3 loop. When light activated, they damage amino acid side chains in the C5 region of Env, as evidenced by inhibition of binding of C5 MAb 9201, but not V3 MAb 13105100. Anionic porphyrins could be used in targeted photodynamic decontamination of biological fluids, such as blood, killing HIV without disabling the function of desirable transfusion products. Dairou *et al.* [2004] (**antibody binding site definition and exposure**)
- 9201: Does not neutralize LAI. This paper notes the peptide binding region is GGGDMRDNWRSE. McDougal *et al.* [1996] (**antibody binding site definition and exposure**)

No. 604
MAb ID 1C1
HXB2 Location gp160 (471–490)
Author Location gp120 (471–490 LAI)
Epitope GGGDMRDNWRSELYKYKVVK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: Env
Species (Isotype) mouse (IgG)
Ab Type C5
Research Contact Repligen Inc, Cambridge, MA, commercial
References Zwick *et al.* 2003; Moore & Sodroski 1996; VanCott *et al.* 1995; Moore *et al.* 1994d; Moore *et al.* 1994c
Keywords antibody interactions

- 1C1: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding MAb that had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)
- 1C1: C5 region linear epitope, binds weakly to nondenatured monomeric gp120 – M91 binding was enhanced by 1C1, but 1C1 binding was inhibited by M91 – non-reciprocal binding enhancement of some C1 and V2 antibodies – non-reciprocal binding inhibition of some CD4 binding site antibodies. Moore & Sodroski [1996]
- 1C1: Linear epitope not exposed on conformationally intact gp120. VanCott *et al.* [1995]
- 1C1: The relative affinity for denatured/native gp120 is 15. Moore *et al.* [1994c]
- 1C1: C2 and V3 regions substitutions can influence binding. Moore *et al.* [1994d]

No. 605
MAb ID 3F5

HXB2 Location gp160 (471–490)
Author Location gp120 (471–490 LAI)
Epitope GGGDMRDNWRSELYKYKVVK
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C5
Research Contact S. Nigida, NCI, USA
References Moore *et al.* 1994c

- 3F5: The relative affinity for denatured/native gp120 is 100. Moore *et al.* [1994c]

No. 606
MAb ID 5F4/1
HXB2 Location gp160 (471–490)
Author Location gp120 (471–490 LAI)
Epitope GGGDMRDNWRSELYKYKVVK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* HIV-2 ROD
Species (Isotype) mouse
Ab Type C5
Research Contact S. Ranjbar, NIBSC, UK
References Moore *et al.* 1994c

- 5F4/1: V5-C5 region – preferentially binds SDS-DTT denatured gp120 (>10 fold) – mutation 485 K/V impairs binding. Moore *et al.* [1994c]

No. 607
MAb ID 660-178
HXB2 Location gp160 (471–490)
Author Location gp120 (471–490 LAI)
Epitope GGGDMRDNWRSELYKYKVVK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: Env
Species (Isotype) mouse (IgG)
Ab Type C5
Research Contact G. Robey, Abbott Labs
References Moore *et al.* 1994d; Moore *et al.* 1994c

- 660-178: The relative affinity for denatured/native gp120 is >100. Moore *et al.* [1994c]
- 660-178: DeltaV1/V2 and DeltaV1/V2/V3 reduce binding – C2 and C5 mutations enhance binding. Moore *et al.* [1994d]

No. 608
MAb ID 9301
HXB2 Location gp160 (471–490)
Author Location gp120 (471–490 LAI)
Epitope GGGDMRDNWRSELYKYKVVK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: Env
Species (Isotype) mouse (IgG)
Ab Type C5
Research Contact Dupont, commercial
References Wagner *et al.* 1996; Moore *et al.* 1994d; Moore *et al.* 1994c; Moore & Ho 1993; Skinner *et al.* 1988b

- 9301: Wagner *et al.* claim that Nea 9301 is anti-V3 – might they have meant MAb 9305? Wagner *et al.* [1996]
- 9301: The relative affinity for denatured/native gp120 is 19. Moore *et al.* [1994d]
- 9301: Bound preferentially to denatured IIIB gp120. Moore & Ho [1993]

No. 609
MAb ID B221 (221)
HXB2 Location gp160 (471–490)
Author Location gp120 (471–490 LAI)
Epitope GGGDMRDNWRSELYKYKVVK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43
HIV component: gp160
Species (Isotype) mouse (IgG1κ)
Ab Type C5
Research Contact Rod Daniels
References Moore *et al.* 1994d; Moore *et al.* 1994c; Bristow *et al.* 1994; Moore & Ho 1993

- B221: UK Medical Research Council AIDS reagent: ARP301.
- B221: MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. Bristow *et al.* [1994]
- B221: The relative affinity for denatured/native gp120 is 12 – mutation 477 D/V impairs binding. Moore *et al.* [1994c]
- B221: Called 221 – C2 and V3 substitutions influence binding. Moore *et al.* [1994d]
- B221: Called 221 – bound preferentially to denatured IIIB gp120. Moore & Ho [1993]

No. 610
MAb ID 8C6/1
HXB2 Location gp160 (471–490)
Author Location gp120 (471–490 LAI)
Epitope GGGDMRDNWRSELYKYKVVK
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI
Species (Isotype) mouse (IgG)
Ab Type V5-C5
Research Contact S. Ranjbar, NIBSC, UK
References Moore *et al.* 1994c

- 8C6/1: UK Medical Research Council AIDS reagent: ARP3052.
- 8C6/1: V5-C5 region – preferentially binds SDS-DTT denatured gp120 (>30 fold) – mutation 485 K/V impairs binding. Moore *et al.* [1994c]

No. 611
MAb ID H11

HXB2 Location gp160 (472–477)
Author Location gp120 (472–477 HXB2)
Epitope GGDMRD
Subtype B
Neutralizing
Immunogen
Species (Isotype) mouse
Ab Type C5
References Pincus *et al.* 1996; Pincus & McClure 1993

- H11: Binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect. Pincus & McClure [1993]; Pincus *et al.* [1996]

No. 612
MAb ID W2
HXB2 Location gp160 (472–491)
Author Location gp120 (472–491 LAI)
Epitope GGDMRDNWRSELYKYKVVKI
Subtype B
Neutralizing
Immunogen Vaccine
Strain: B clade LAI *HIV component:* Env
Species (Isotype) mouse (IgG)
Ab Type C5
Research Contact D. Weiner, U. Penn., USA
References Moore *et al.* 1994c

- W2: The relative affinity for denatured/native gp120 is 30 – mutation 485 K/V impairs binding. Moore *et al.* [1994c]

No. 613
MAb ID M38
HXB2 Location gp160 (485–504)
Author Location gp120 (490–508)
Epitope KYKVVKEIPLGVAPTKAKRR
Neutralizing no
Immunogen Vaccine
Vector/Type: virus *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse
Ab Type C5
References Maksiutov *et al.* 2002; Beretta & Dalgleish 1994; DeSantis *et al.* 1994; Lopalco *et al.* 1993; Grassi *et al.* 1991; Beretta *et al.* 1987

- M38: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV, as well as to a fragment of IFN-related IFRD2 (PC4-B) protein, ARTKARSRVRDKRA. Maksiutov *et al.* [2002]
- M38: Infected individuals have HLA class I-gp120 cross-reactive antibodies. DeSantis *et al.* [1994]
- M38: Binds to the carboxy terminus of gp120, in a gp41 binding region, and also to denatured human HLAs (antigenic homology) Lopalco *et al.* [1993]
- M38: Binds to gp120 and to a 80 kd human protein expressed on a small fraction of mononuclear cells in the lymph nodes. Beretta *et al.* [1987]

No. 614
MAb ID Chim 1 (C-1)
HXB2 Location gp160 (487–493)
Author Location gp120 (492–498 HXB2)
Epitope KVVKEIP
Subtype B
Neutralizing
Immunogen
Species (Isotype) humanized chimpanzee
References Pincus *et al.* 1996; Pincus & McClure 1993

- Chim 1: Binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect. Pincus & McClure [1993]; Pincus *et al.* [1996]

No. 615
MAb ID polyclonal
HXB2 Location gp160 (490–511)
Author Location gp120 (495–516 BRU)
Epitope KIEPLGVAPTKAKRRVVQREKR
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human
References Maksiutov *et al.* 2002; Hernandez *et al.* 2000

- This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV, as well as to a fragment of IFN-related IFRD2 (PC4-B) protein, ARTKARSRVRDKRA. Maksiutov *et al.* [2002]
- Chimeric peptide combining two peptides gp160(495-516 and 584-612) served as a specific and broadly reactive antigen for diagnostic detection of HIV-1. Hernandez *et al.* [2000]

No. 616
MAb ID 110.1
HXB2 Location gp160 (491–500)
Author Location gp120 (491–500 LAI)
Epitope IEPLGVAPTK
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1
Species (Isotype) mouse (IgG1κ)
Ab Type C5
Research Contact Genetic Systems Corp, Seattle WA, E. Kinney-Thomas
References Maksiutov *et al.* 2002; Valenzuela *et al.* 1998; Binley *et al.* 1997a; McDougal *et al.* 1996; Cook *et al.* 1994; Moore *et al.* 1994c; Callahan *et al.* 1991; Pincus *et al.* 1991; Thomas *et al.* 1988; Linsley *et al.* 1988; Gosting *et al.* 1987
Keywords antibody binding site definition and exposure, immunotoxin

- 110.1: There is another antibody with this ID that binds to gp120, but at aa 200-217.
- 110.1: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV. Maksiutov *et al.* [2002]
- 110.1: Does not effect LAI viral binding or entry into CEM cells. Valenzuela *et al.* [1998]
- 110.1: Does not neutralize HIV-1 LAI. McDougal *et al.* [1996]

- 110.1: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the carboxy-terminus of gp120 inhibit gp120 binding to GalCer but not as potently as anti-V3 MAbs – binding of GalCer to gp120 does not inhibit MAb binding. Cook *et al.* [1994]
- 110.1: The relative affinity for denatured/native gp120 is 0.7. Moore *et al.* [1994c] (**antibody binding site definition and exposure**)
- 110.1: Polyanionic polysaccharides were proposed to inhibit viral functions such as binding and syncytia formation through interations mediated through the local high positive charge density in the V3 loop. The binding of this antibody is not inhibited by dextransulfate, in contrast to anti-V3 antibodies. Callahan *et al.* [1991]
- 110.1: Difference was noted in the epitope: mapped to aa 421-429 (KQIINMWQE), the T1 sequence – poor efficacy as an immunotoxin when linked to RAC. Pincus *et al.* [1991] (**antibody binding site definition and exposure**, **immunotoxin**)
- 110.1: Referred to as 110-1 – does not inhibit CD4-gp120 binding or neutralize HIV-1 strains. Linsley *et al.* [1988]

No. 617
MAb ID 42F
HXB2 Location gp160 (491–500)
Author Location gp120 (491–500 HXB2)
Epitope IEPLGVAPTK
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type C5
References Maksiutov *et al.* 2002; Alsmadi & Tilley 1998; Alsmadi *et al.* 1997

- 42F: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV. Maksiutov *et al.* [2002]
- 42F: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against strains IIIB, MN, SF-2, and RF, but not a clone of MN. Alsmadi & Tilley [1998]
- 42F: 42F and 43F were isolated from a long term non-progressor by EBV transformation of PBMC – samples were taken 14 months apart – both MAbs stained diverse strains of infected cells and directed ADCC – were more potent for ADCC if the cell was infected with HIV-1, rather than just presenting absorbed gp120. Alsmadi *et al.* [1997]

No. 618
MAb ID 43F
HXB2 Location gp160 (491–500)
Author Location gp120 (491–500 HXB2)
Epitope IEPLGVAPTK
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type C5
References Maksiutov *et al.* 2002; Alsmadi *et al.* 1997

- 43F: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV. Maksiutov *et al.* [2002]
- 43F: 42F and 43F were isolated from a long term non-progressor by EBV transformation of PBMC – samples were taken 14 months apart – both MAbs stained diverse strains of infected cells and directed ADCC – were more potent for ADCC if the cell was infected with HIV-1, rather than just presenting absorbed gp120. Alsmadi *et al.* [1997]

No. 619
MAb ID RV110026
HXB2 Location gp160 (491–500)
Author Location gp120 (491–500 LAI)
Epitope IEPLGVAPTK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade LAI
Species (Isotype) human
Ab Type C5
Research Contact Commercial, Olympus Inc
References Maksiutov *et al.* 2002; Moore *et al.* 1994d; Moore *et al.* 1994c

- RV110026: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV. Maksiutov *et al.* [2002]
- RV110026: Preferentially binds SDS-DTT denatured gp120 (15 fold using R1/87 as capture reagent) Moore *et al.* [1994c]

No. 620
MAb ID 105-306
HXB2 Location gp160 (492–500)
Author Location gp120 (498–505 HAM112, O group)
Epitope KPFSVAPTP
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* O group HAM112 *HIV component:* gp160
Species (Isotype) mouse (IgG1κ)
Ab Type C-term
References Scheffel *et al.* 1999

- 105-306: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – 105-306 bound to two overlapping peptides. Scheffel *et al.* [1999]

No. 621
MAb ID GV1G2
HXB2 Location gp160 (494–499)
Author Location gp120 (494–499 IIIB)
Epitope LGVAPT
Neutralizing
Immunogen Vaccine
Vector/Type: protein-Ab complex *HIV component:* gp120-Mab complex
Species (Isotype) mouse
Ab Type C5
References Denisova *et al.* 1996

- GV1G2: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes – MAbs GV12F6 and GV3H1 are homologous to GV1G2 and were generated in the same experiment. Denisova *et al.* [1996]

No. 622
MAb ID 750-D
HXB2 Location gp160 (498–504)
Author Location gp120 (503–509)
Epitope PTKAKRR
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG3λ)
Ab Type C-term
References Hioe *et al.* 2000; Forthal *et al.* 1995

- 750-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C5 MAbs 450-D and 750-D did not effect proliferation. Hioe *et al.* [2000]
- 750-D: Not neutralizing, positive ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995]

No. 623
MAb ID 450-D (450-D-3, 450D)
HXB2 Location gp160 (498–504)
Author Location gp120 (475–486 BH10)
Epitope PTKAKRR(orRRVVQRE,orMRDNWRSELYKY-dependingonreference)
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type C5
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Verrier *et al.* 2001; Hioe *et al.* 2001; Hioe *et al.* 2000; Hioe *et al.* 1997b; Li *et al.* 1997; Manca *et al.* 1995a; Forthal *et al.* 1995; Cook *et al.* 1994; Gorny *et al.* 1994; Laal *et al.* 1994; Spear *et al.* 1993; Karwowska *et al.* 1992b; Karwowska *et al.* 1992a; Durda *et al.* 1988

- 450-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFN gamma production – 450-D does not have this effect and was used as a control in this study. Hioe *et al.* [2001]
- 450-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001]
- 450-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C5 MAbs 450-D and 750-D did not effect proliferation. Hioe *et al.* [2000]
- 450-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b]
- 450-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 6 mug/ml. Li *et al.* [1997]
- 450-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995]
- 450-D: Virions complexed to gp120 Ab facilitate presentation of p66 RT epitopes to Th cells. Manca *et al.* [1995a]
- 450-D: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the carboxy-terminus of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. Cook *et al.* [1994]
- 450-D: Epitope is defined as PTKAKRR. Gorny *et al.* [1994]
- 450-D: Not neutralizing alone, could synergize anti-CD4 binding site antibody neutralization. Laal *et al.* [1994]
- 450-D: Did not mediate deposition of complement component C3 on HIV infected cells. Spear *et al.* [1993]
- 450-D: Bound to MN, SF-2 and IIIB, but was not neutralizing. Karwowska *et al.* [1992a]

No. 624
MAb ID 670-D (670)
HXB2 Location gp160 (498–504)
Author Location gp120 (503–509)
Epitope PTKAKRR
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type C5
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY
References Zwick *et al.* 2003; Verrier *et al.* 2001; Nyambi *et al.* 2000; Gorny & Zolla-Pazner 2000; Altmeyer *et al.* 1999; Nyambi *et al.* 1998; Gorny *et al.* 1998; Hioe *et al.* 1997b; Gorny *et al.* 1997; Hill *et al.* 1997; Forthal *et al.* 1995; Zolla-Pazner *et al.* 1995
Keywords antibody interactions

- 670-D: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and

V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding MAb that had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)

- 670-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001]
- 670-D: A gp120 C5 MAb used as a negative control in a study of anti-gp41 MAbs. Gorny & Zolla-Pazner [2000]
- 670-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 670-D bound 21/26, and was the most cross-reactive C5 MAb. Nyambi *et al.* [2000]
- 670-D: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies. Altmeyer *et al.* [1999]
- 670-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-C5 Abs 670-D and 1331A bound to 3/4 B clade viruses (they didn't bind to IIIB), and to subtype D MAL – 670-D also reacted with subtype A. Nyambi *et al.* [1998]
- 670-D: gp120 can inhibit MIP-1alpha from binding to CCR5, but this inhibitory effect is blocked by pre-incubation of gp120 with three anti-V3 MAbs: 447, 257, 1027 – MAb 670 which binds in the C5 region had no effect. Hill *et al.* [1997]
- 670-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b]
- 670-D: Not neutralizing, positive ADCC activity, and no viral enhancing activity, numbering provided suggests epitope is RRVVQRE. Forthal *et al.* [1995]
- 670-D: Group specific cross-clade binding in serotyping study using flow-cytometry. Zolla-Pazner *et al.* [1995]

No. 625
MAb ID 158F3
HXB2 Location gp160 (499–511)
Author Location gp120 (BaL)
Epitope TKAKRRVVQREKR
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: gp120-CD4 complex *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) humanized mouse (IgG2κ)
Ab Type C-term
Research Contact Abraham Pinter, Lab. of Retrovirology, Public Research Institute, pinter@phri.org
References He *et al.* 2003
Keywords antibody binding site definition and exposure, vaccine antigen design

- 158F3: Vaccination of a gp120-CD4 fusion complex in six transgenic XMG2 XenoMouse mice that produce human IgG2 with K light chain did not produce any neutralizing antibodies. 36/39 MAbs derived from one of these mice were in one of two competition groups that were conformational and specific for the complex, suggesting this chimeric vaccine may be of little value, as immunodominant responses are to epitopes unique to the complex, not present in native Env. This MAb is one of the 3/36 non-neutralizing MAbs that bound to linear epitopes on gp120. He *et al.* [2003] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 626
MAb ID 161D7
HXB2 Location gp160 (499–511)
Author Location gp120 (BaL)
Epitope TKAKRRVVQREKR
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: gp120-CD4 complex *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) humanized mouse (IgG2κ)
Ab Type C-term
Research Contact Abraham Pinter, Lab. of Retrovirology, Public Research Institute, pinter@phri.org
References He *et al.* 2003
Keywords antibody binding site definition and exposure, vaccine antigen design

- 161D7: Vaccination of a gp120-CD4 fusion complex in six transgenic XMG2 XenoMouse mice that produce human IgG2 with K light chain did not produce any neutralizing antibodies. 36/39 MAbs derived from one of these mice were in one of two competition groups that were conformational and specific for the complex, suggesting this chimeric vaccine may be of little value, as immunodominant responses are to epitopes unique to the complex, not present in native Env. This MAb is one of the 3/36 non-neutralizing MAbs that bound to linear epitopes on gp120. He *et al.* [2003] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 627
MAb ID polyclonal
HXB2 Location gp160 (503–509)

Author Location gp120 (471–477)
Epitope RRVVQRE
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp120
Species (Isotype) mouse (IgG)
References Jeyarajah *et al.* 1998

- Mice were immunized with peptide APTKAKRRVVQREKR – epitope excision and extraction combined with mass spectrometry was used to map the fine structure of epitopes recognized by polyclonal Ab to HIV-1 Env – a major epitope was identified between positions 472 and 478. Jeyarajah *et al.* [1998]

No. 628
MAb ID 722-D
HXB2 Location gp160 (503–509)
Author Location gp120 (503–509)
Epitope RRVVQRE
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type C-term
References Forthal *et al.* 1995; Laal *et al.* 1994

- 722-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995]
- 722-D: Not neutralizing alone, could synergize anti-CD4 binding site antibody neutralization. Laal *et al.* [1994]

No. 629
MAb ID polyclonal
HXB2 Location gp160 (503–511)
Author Location gp120 (508–516)
Epitope RRVVQREKR
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type C-term
References Loomis-Price *et al.* 1997; Palker *et al.* 1987

- Most HIV-1 + individuals have an antibody response to this epitope – in this study, reactivity to RRVVQREKR was used as a positive control for HIV-1 + gp160 vaccine recipients. Loomis-Price *et al.* [1997]

No. 630
MAb ID 1131-A
HXB2 Location gp160 (505–511)
Author Location gp120 (510–516 LAI)
Epitope VVQREKR
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG3λ)
Ab Type C-term
References Bandres *et al.* 1998

- 1131-A: A very high affinity antibody used in studies that demonstrate that CXCR4 can bind to gp120 in the absence of CD4-gp120 interactions, and that this binding can be enhanced by Env deglycosylation. Bandres *et al.* [1998]

No. 631
MAb ID 858-D
HXB2 Location gp160 (505–511)
Author Location gp120 (510–516 LAI)
Epitope VVQREKR
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
Ab Type C-term
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Nyambi *et al.* 2000; Gorny *et al.* 2000; Forthal *et al.* 1995; Zolla-Pazner *et al.* 1995

- 858-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – C5 MAbs 858-D, 989-D and 1331A bound with a 5-10 fold preference for the monomer. Gorny *et al.* [2000]
- 858-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 858-D bound only 4/26, the worst of all anti-C5 MAbs tested, while MAb 1331A, which shares the same core epitope (positions 495-516), bound to 18/26 isolates. Nyambi *et al.* [2000]
- 858-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995]
- 858-D: Group specific cross-clade binding in serotyping study using flow-cytometry. Zolla-Pazner *et al.* [1995]

No. 632
MAb ID 989-D
HXB2 Location gp160 (505–511)
Author Location gp120 (LAI)
Epitope VVQREKR
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
Ab Type C-term
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Nyambi *et al.* 2000; Gorny *et al.* 2000; Zolla-Pazner *et al.* 1995

- 989-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – C5 MAbs 858-D, 989-D and 1331A bound with a 5-10 fold preference for the monomer. Gorny *et al.* [2000]
- 989-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 989-D bound to 6/26 isolates. Nyambi *et al.* [2000]
- 989-D: In serotyping study using flow-cytometry, showed B clade specificity, but only reacted with 7/11 B clade virus. Zolla-Pazner *et al.* [1995]

No. 633
MAb ID 1331A
HXB2 Location gp160 (505–511)
Author Location gp120 (510–516)
Epitope dwVVQREKR
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG3λ)
Ab Type C5
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Zwick *et al.* 2003; Edwards *et al.* 2002; Gorny *et al.* 2002; Nyambi *et al.* 2000; Hochleitner *et al.* 2000b; Gorny *et al.* 2000; Nyambi *et al.* 1998

- 1331A: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding MAb that had no impact on 4KG5 binding. Zwick *et al.* [2003]
- 1331A: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. Edwards *et al.* [2002]
- 1331A: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions and the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control as binding was not diminished by treating gp120 with DTT or sodium metaperiodate to reduce disulfide bonds), and MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) Gorny *et al.* [2002]
- 1331A: Core epitope dwVVQREKR maps to gp120(510-516) – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – C5 MAbs 858-D, 989-D and 1331A bound with a 5-10 fold preference for the monomer. Gorny *et al.* [2000]
- 1331A: The Ab binding site was studied with epitope excision (protein is bound in native conformation to immobilized MAb, then digested with proteolytic enzymes) and extraction (protein is digested then allowed to react with Ab), followed by mass spectroscopy – two non-contiguous aa in C5 were protected, E-507 and I-487, which are thought to be located on opposite sides of hydrophobic pocket involved in gp120/gp41 interaction. Hochleitner *et al.* [2000b]
- 1331A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 858-D bound only 4/26, the worst of all anti-C5 MAbs tested, while MAb 1331A, which shares the same core epitope (positions 495-516), bound to 18/26. Nyambi *et al.* [2000]
- 1331A: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-C5 Abs 670-D and 1331A bound to 3/4 B clade viruses (they don't bind to IIIB), and to subtype D MAL. Nyambi *et al.* [1998]

No. 634
MAb ID 1A1
HXB2 Location gp160 (525–543)
Author Location gp41 (526–543 BH10)
Epitope AAGSTMGAASMTLTVQARQ
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Maksiutov *et al.* 2002; Buchacher *et al.* 1994

- 1A1: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV. Maksiutov *et al.* [2002]
- 1A1: Human MAb generated using EBV transformation of PBL from HIV-1 + volunteers. Buchacher *et al.* [1994]

No. 635
MAb ID 24G3
HXB2 Location gp160 (525–543)
Author Location gp41 (526–543 BH10)
Epitope AAGSTMGAASMTLTVQARQ
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Maksiutov *et al.* 2002; Buchacher *et al.* 1994; Buchacher *et al.* 1992

- 24G3: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV. Maksiutov *et al.* [2002]
- 24G3: Human MAb generated by electrofusion of PBL from HIV-1 + volunteers with CB-F7 cells. Buchacher *et al.* [1994]

No. 636
MAb ID 25C2 (IAM 41-25C2)
HXB2 Location gp160 (525–543)
Author Location gp41 (526–543 BH10)
Epitope AAGSTMGAASMTLTVQARQ

Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria and Viral Testing Systems, Houston, TX
References Maksiutov *et al.* 2002; Sattentau *et al.* 1995; Buchacher *et al.* 1994; Buchacher *et al.* 1992

- 25C2: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV. Maksiutov *et al.* [2002]
- 25C2: Called IAM 41-25C2 – Binding domain overlaps sites that are critical for gp120-gp41 association – binding is enhanced by sCD4 – binding region defined as: gp41(21-38 BH10) Sattentau *et al.* [1995]
- 25C2: Human MAb generated by electrofusion of PBL from HIV-1 + volunteers with CB-F7 cells – binds oligomeric and monomeric gp41, and gp160. Buchacher *et al.* [1994]

No. 637
MAb ID 5F3
HXB2 Location gp160 (525–543)
Author Location gp41 (526–543 BH10)
Epitope AAGSTMGAASMTLTVQARQ
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Maksiutov *et al.* 2002; Buchacher *et al.* 1994

- 5F3: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV. Maksiutov *et al.* [2002]
- 5F3: Human MAb generated by electrofusion of PBL from HIV-1 + volunteers with CB-F7 cells. Buchacher *et al.* [1994]

No. 638
MAb ID α(566-586)
HXB2 Location gp160 (561–581)
Author Location gp41 (566–586 BRU)
Epitope AQQHLLQLTVWGIKQLQARIL
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Poumbourios *et al.* 1992

No. 639
MAb ID PC5009
HXB2 Location gp160 (572–591)
Author Location gp41 (577–596 BRU)
Epitope GIKQLQARILAVERYLKDQQ
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (Isotype) mouse
References Poumbourios *et al.* 1992

- PC5009: Recognized only monomeric gp41. Poumbourios *et al.* [1992]

No. 640
MAb ID polyclonal α577-596
HXB2 Location gp160 (572–591)
Author Location gp41 (577–596 BRU)
Epitope GIKQLQARILAVERYLKDQQ
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Poumbourios *et al.* 1992

- alpha(577-596): Affinity purified from HIV-1 + plasma – preferentially bind oligomer. Poumbourios *et al.* [1992]

No. 641
MAb ID polyclonal
HXB2 Location gp160 (576–592)
Author Location gp41 (583–599)
Epitope LQARILAVERYLKDQQL
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Klasse *et al.* 1993b

- 42 HIV-1 positive human sera were tested against wildtype peptide, and peptide with substitution 589 A to T: 11/42 reacted strongly with wildtype, weakly with A589T – 31 reacted weakly with parental, even more weakly with substituted. Klasse *et al.* [1993b]

No. 642
MAb ID
HXB2 Location gp160 (577–583)
Author Location gp41 (582–589)
Epitope QARILAV
Subtype B
Neutralizing yes
Immunogen HIV-1 exposed seronegative
Species (Isotype) human (IgA)
Ab Type Leucine zipper motif
References Clerici *et al.* 2002a

- Six sera from HIV-exposed uninfected individuals(EU), HIV-infected individuals and healthy controls were analyzed for IgA Abs – neutralizing activity was observed with total IgA from both EU and HIV+ – the EU IgA exclusively bound to a distinctive epitope within gp41, QARILAV, in the coiled coil pocket important for gp120-gp41 interactions – sera of QAFILAV-immunized BALB/c mice was neutralizing with the dose-dependent behavior similar to 2F5. Clerici *et al.* [2002a]

No. 643
MAb ID
HXB2 Location gp160 (577–583)
Author Location gp41 (582–589)
Epitope QARILAV
Subtype B
Neutralizing yes
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41 *Adjuvant:* Keyhole Limpit Haemocyanin (KLH)
Species (Isotype) mouse (IgA)
Ab Type Leucine zipper motif

References Clerici *et al.* 2002a

- Six sera from HIV-exposed uninfected individuals(EU), HIV-infected individuals and healthy controls were analyzed for IgA Abs – neutralizing activity was observed with total IgA from both EU and HIV+ – the EU IgA exclusively bound to a distinctive epitope within gp41, QARILAV – sera of QAFILAV-immunized BALB/c mice was neutralizing with the dose-dependent behavior similar to 2F5. Clerici *et al.* [2002a]

No. 644
MAb ID 1F11
HXB2 Location gp160 (578–612)
Author Location gp41 (579–613 BH10)
Epitope ARILAVERYLKDQQLLGIWGCSGKLICTTAVP-WNA
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Gorny & Zolla-Pazner 2004; Buchacher *et al.* 1994; Buchacher *et al.* 1992
Keywords antibody generation, review

- 1F11: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 1F11: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994] (**antibody generation**)

No. 645
MAb ID 1H5
HXB2 Location gp160 (578–612)
Author Location gp41 (579–613 BH10)
Epitope ARILAVERYLKDQQLLGIWGCSGKLICTTAVP-WNA
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Gorny & Zolla-Pazner 2004; Buchacher *et al.* 1994; Buchacher *et al.* 1992
Keywords antibody generation, review

- 1H5: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 1H5: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994] (**antibody generation**)

No. 646
MAb ID 3D9
HXB2 Location gp160 (578–612)
Author Location gp41 (579–613 BH10)
Epitope ARILAVERYLKDQQLLGIWGCSGKLICTTAVP-WNA
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Gorny & Zolla-Pazner 2004; Buchacher *et al.* 1994; Buchacher *et al.* 1992
Keywords antibody generation, review

- 3D9: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 3D9: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994] (**antibody generation**)

No. 647
MAb ID 4B3
HXB2 Location gp160 (578–612)
Author Location gp41 (579–613 BH10)
Epitope ARILAVERYLKDQQLLGIWGCSGKLICTTAVP-WNA
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Gorny & Zolla-Pazner 2004; Chen *et al.* 1994b; Buchacher *et al.* 1994; Buchacher *et al.* 1992
Keywords antibody generation, review

- 4B3: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 4B3: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994] (**antibody generation**)

No. 648
MAb ID 4D4
HXB2 Location gp160 (578–612)
Author Location gp41 (579–613 BH10)
Epitope ARILAVERYLKDQQLLGIWGCSGKLICTTAVP-WNA
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria and Viral Testing Systems, Houston, TX
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1999; Sattentau *et al.* 1995; Chen *et al.* 1994b; Buchacher *et al.* 1994; Buchacher *et al.* 1992
Keywords antibody binding site definition and exposure, antibody generation, review, vaccine antigen design

- 4D4: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)

- 4D4: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 4D4: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994] (**antibody generation**)

No. 649
MAb ID 4G2
HXB2 Location gp160 (578–612)
Author Location gp41 (579–613 BH10)
Epitope ARILAVERYLKDQQLLGIWGCSGKLICTTAVP-WNA
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Gorny & Zolla-Pazner 2004; Buchacher *et al.* 1994; Buchacher *et al.* 1992
Keywords antibody generation, review

- 4G2: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 4G2: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994] (**antibody generation**)

No. 650
MAb ID polyclonal
HXB2 Location gp160 (579–589)
Author Location gp41 (586–596 IIIB)
Epitope RILAVERYLKD
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41 *Adjuvant:* BSA
Species (Isotype) rabbit, mouse
Ab Type C-domain
References Xiao *et al.* 2000b

- Strong epitope-specific neutralizing antibody responses were induced using the peptide C(RILAVERYLKD)_2-BSA, but not full gp160. Xiao *et al.* [2000b]

No. 651
MAb ID polyclonal
HXB2 Location gp160 (579–589)
Author Location gp41 (586–596)
Epitope RILAVERYLKD
Neutralizing
Immunogen Vaccine
Vector/Type: protein, polyepitope *HIV component:* gp160 *Adjuvant:* BSA
Species (Isotype) rabbit
Ab Type N-term
References Lu *et al.* 2000b; Lu *et al.* 2000c

- High titer response to ELDKWA and RILAVERYLKD was observed upon vaccination with multiple-epitope vaccine CG-GPGRAFY-G-ELDKWA-G-RILAVERYLKD conjugated to BSA, a weak response to GPGRAFY – immunization with CG-(ELDKWA-GPGRAFY)_2-K was also tried, yielding a strong Ab response to both ELDKWA and GPGRAFY – gp160 vaccination yielded strong Ab response but not to any of the peptides studied here. Lu *et al.* [2000c,b]

No. 652
MAb ID
HXB2 Location gp160 (579–599)
Author Location gp41 (586–606)
Epitope RILAVERYLKDQQLLGIWGCS
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Wang *et al.* 1986
Keywords assay standardization/improvement

- Immunoabsorbant peptide antigen RIAVERYLKDQQLLGI-WGCS was used in a solid-phase enzyme immunoassay (EIA)to detect gp41-specific Abs in sera of virtually all HIV-1 infected individuals tested, with no false positives. This one 21 amino acid long peptide is recognized by sera from almost all AIDS patients, can be easily synthesized and employed for serological testing for HIV infection. Wang *et al.* [1986] (**assay standardization/improvement**)

No. 653
MAb ID polyclonal
HXB2 Location gp160 (579–599)
Author Location gp41 (583–604)
Epitope RILAVERYLKDQQLLGIWGCS
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* desialylated gp160
Species (Isotype) rabbit
References Benjouad *et al.* 1993

- MAbs raised against desialylated HIV-1 gp160 cross-react with HIV-2 gp140 due to immunodominant conserved epitope in gp41. Benjouad *et al.* [1993]

No. 654
MAb ID 2A2/26
HXB2 Location gp160 (579–601)
Author Location gp41 (584–606 BRU)

Epitope RILAVERYLKDQQLLGIWGCSGK
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp41
Species (Isotype) mouse (IgG)
References Poumbourios *et al.* 1995; Poumbourios *et al.* 1992

- 2A2/26: Delta 550-561 (Delta LLRAIEAQQHLL), a region important for oligomer formation diminishes binding, Delta (550-561 +571-581) abrogates binding. Poumbourios *et al.* [1995]
- 2A2/26: Immunodominant region, binds both oligomer and monomer. Poumbourios *et al.* [1992]

No. 655
MAb ID 50-69 (SZ-50.69, 50-69D)
HXB2 Location gp160 (579–603)
Author Location gp41 (579–603 BH10)
Epitope RILAVERYLKDQQLLGIWGCSGKLI
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG2κ)
Ab Type cluster I
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY
References McCaffrey *et al.* 2004; Ling *et al.* 2004; Gorny & Zolla-Pazner 2004; Finnegan *et al.* 2002; Follis *et al.* 2002; Verrier *et al.* 2001; Zwick *et al.* 2001b; Nyambi *et al.* 2000; Gorny *et al.* 2000; Gorny & Zolla-Pazner 2000; Mitchell *et al.* 1998; Hioe *et al.* 1997b; Boots *et al.* 1997; Stamatatos *et al.* 1997; Klasse & Sattentau 1996; Binley *et al.* 1996; Poignard *et al.* 1996a; McDougal *et al.* 1996; Manca *et al.* 1995a; Sattentau *et al.* 1995; Chen *et al.* 1995; Laal *et al.* 1994; Spear *et al.* 1993; Eddleston *et al.* 1993; Sattentau & Moore 1991; Robinson *et al.* 1991; Xu *et al.* 1991; Gorny *et al.* 1989; Pinter *et al.* 1989; Till *et al.* 1989
Keywords antibody binding site definition and exposure, antibody interactions, complement, enhancing activity, immunotoxin, inter-clade comparisons, kinetics, mimotopes, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- 50-69: NIH AIDS Research and Reference Reagent Program: 531.
- 50-69: This is one of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 50-69: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of 17b and F105 was decreased by trypsin, but increased by thrombin. gp41 MAbs 246D, 98.6, 50-69, were decreased by trypsin, unaltered by thrombin, while NAb 2F5 binding was increased by thrombin. Thrombin may increase HIV-induced cell fusion in blood by causing a conformational activating shift in gp120. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 50-69: Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. SF162 and each of the five glycosyation mutants studied were all neutralization resistant to 50-69. V3 glycans tended to shield V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans shielded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 50-69: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. Finnegan *et al.* [2002] (**antibody binding site definition and exposure**, **kinetics**)
- 50-69: Called 50-69D. Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. Follis *et al.* [2002] (**antibody binding site definition and exposure**)
- 50-69: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between

gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001] (**antibody interactions**)
- 50-69: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – MAb 50-69 binding to infected cells is enhanced by sCD4, while 4E10 and Z13 binding is essentially unaltered. Zwick *et al.* [2001b] (**antibody binding site definition and exposure**)
- 50-69: A cluster I epitope that binds to rgp41 567-647, recognizes a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41 – this MAb doesn't react with either of the peptides N51 or C43 individually – MAbs 50-69 and 1367 had similar properties – MAb 50-69 bound the fusogenic form of the protein in liquid phase. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**)
- 50-69: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)
- 50-69: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 50-69 bound the majority of isolates although binding was moderate to weak – specifies discontinuous binding site range as aa 579-613. Nyambi *et al.* [2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 50-69: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613 – identifies noncontiguous W596-G597-C598 and C604-T605 as minimal epitope. Mitchell *et al.* [1998] (**antibody binding site definition and exposure**)
- 50-69: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – 50-69 maps to an immunodominant domain in gp41 – three groups of peptides were selected, one which seems most closely related to gp41 sequence peptide consensus is WGCxx(RK)(x n)LxC – the analogous gp41 sequence WGCSGKLIC is present in most M group clades, except D with a common L to H substitution. Boots *et al.* [1997] (**mimotopes**)
- 50-69: Binding of anti-gp120 MAbs IgG1b12 or 654-30D does not mediate significant exposure of the gp41 epitopes for MAbs 2F5 and 50-69. Stamatatos *et al.* [1997] (**antibody interactions**)
- 50-69: Binds to a linear epitope located in the cluster I region – binding of 50-69 and 240-D inhibited by Fabs A1, A4, M8B, M26B, M12B and T2. Binley *et al.* [1996] (**antibody binding site definition and exposure**)
- 50-69: Used to test exposure of gp41 upon sCD4 binding. Klasse & Sattentau [1996]
- 50-69: Does not neutralize HIV-1 LAI. McDougal *et al.* [1996] (**variant cross-recognition or cross-neutralization**)
- 50-69: Prebinding of anti-V3, and CD4i MAbs 48d and 17b, but not anti-V2 neutralizing MAbs, expose the 50-69 epitope. Poignard *et al.* [1996a] (**antibody interactions**)
- 50-69: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation. Chen *et al.* [1995] (**antibody binding site definition and exposure**)
- 50-69: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells. Manca *et al.* [1995a]
- 50-69: Preferentially binds oligomer – binding increased after pretreatment of infected cells with sCD4 – binding domain overlaps site that is critical for gp120-gp41 association. Sattentau *et al.* [1995] (**antibody binding site definition and exposure**)
- 50-69: Epitope described as cluster I, 601-604, conformational – does not neutralize IIIB or synergize neutralization by anti-V3 MAb 447-52D or by CD4 BS MAbs. Laal *et al.* [1994] (**antibody binding site definition and exposure**, **antibody interactions**)
- 50-69: Called SZ-50.69 – binds to an epitope within aa 579-613. Eddleston *et al.* [1993] (**antibody binding site definition and exposure**)
- 50-69: Did not mediate deposition of complement component C3 on HIV infected cells unless cells were pre-incubated with sCD4 – complement mediated virolysis of MN and IIIB in the presence of sCD4. Spear *et al.* [1993] (**complement**)
- 50-69: Enhances HIV-1 infection *in vitro* – synergizes with huMAb 120-16 *in vitro* to enhance HIV-1 infection to level approaching that found in polyclonal anti-HIV serum. Robinson *et al.* [1991] (**antibody interactions**, **enhancing activity**)
- 50-69: Two fold increase in binding to gp120 in the presence of bound sCD4. Sattentau & Moore [1991] (**antibody binding site definition and exposure**)
- 50-69: The epitope is affected by the conformation conferred by the two cysteines at amino acids 598 and 604. Xu *et al.* [1991] (**antibody binding site definition and exposure**)
- 50-69: Kills HIV-infected cells when coupled to deglycosylated ricin A chain. Gorny *et al.* [1989] (**immunotoxin**)
- 50-69: Reacts preferentially with gp160 oligomer, compared to gp41 monomer. Pinter *et al.* [1989] (**antibody binding site definition and exposure**)
- 50-69: Combined with deglycosylated A chain of ricin is toxic to lines of HIV-infected T cells (H9) and monocytes (U937) Till *et al.* [1989] (**immunotoxin**)

No. 656
MAb ID 9-11
HXB2 Location gp160 (579–604)
Author Location gp41 (584–609)
Epitope RILAVERYLKDQQLLGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (Isotype) mouse (IgG1)
References Mani *et al.* 1994
- 9-11: required the C-C disulfide bridge and loop formation, can bind simultaneously with 41-1. Mani *et al.* [1994]

No. 657

MAb ID 98-43
HXB2 Location gp160 (579–604)
Author Location gp41 (579–604 HXB2)
Epitope RILAVERYLKDQQLLGIWGCSGKLIC
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG2κ)
References Xu *et al.* 1991; Tyler *et al.* 1990; Gorny *et al.* 1989; Pinter *et al.* 1989

- 98-43: NIH AIDS Research and Reference Reagent Program: 1241.
- 98-43: 579-604 binds in the immunodominant region. Xu *et al.* [1991]
- 98-43: Poor ADCC (in contrast to MAb 120-16, gp41(644-663)) Tyler *et al.* [1990]
- 98-43: Reacts equally well with oligomer and monomer. Pinter *et al.* [1989]

No. 658
MAb ID 41-1 (41.1)
HXB2 Location gp160 (579–608)
Author Location gp41 (584–609)
Epitope RILAVERYLKDQQLLGIWGCSGKLICTTAV
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (Isotype) mouse (IgG1κ)
References Pincus *et al.* 1998; Pincus *et al.* 1996; Mani *et al.* 1994; Pincus & McClure 1993; Pincus *et al.* 1991; Dalgleish *et al.* 1988; Gosting *et al.* 1987

- 41-1: Also called 41.1, although possibly not, the literature is confusing because two gp41 MAbs that bind to this region with similar names (dash versus period) are listed as murine and human.
- 41-1: Called 41.1, and described as a human MAb, binding 579-604 – a panel of immunotoxins was generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. Pincus *et al.* [1996]
- 41-1: This antibody to gp41(584-609) Mani *et al.* [1994] seems to have been named the same as a different MAb to gp41(735-752 IIIB) Dalgleish *et al.* [1988]. Dalgleish *et al.* [1988]; Mani *et al.* [1994]
- 41-1: Did not require the C-C disulfide bridge and loop formation, can bind simultaneously with 9-11. Mani *et al.* [1994]
- 41-1: Called 41.1, and described as a human MAb – cross-competes with 41.4 – sCD4 enhances the efficacy of immunotoxins *in vitro* 30-fold – MAb was coupled to ricin A chain (RAC) Pincus & McClure [1993]
- 41-1: Efficacious as an immunotoxin when coupled to RAC – gave linear epitope as gp160 579-603. Pincus *et al.* [1991]
- 41-1: This antibody seems to have been named the same as a different MAb to gp41(735-752) Dalgleish *et al.* [1988]
- 41-1: Broadly reactive. Gosting *et al.* [1987]

No. 659
MAb ID 41.4
HXB2 Location gp160 (579–608)
Author Location gp41 (584–609)
Epitope RILAVERYLKDQQLLGIWGCSGKLICTTAV
Neutralizing
Immunogen
Species (Isotype)
Research Contact Jan McClure, Bristol-Myers Squibb Pharmaceutical Res Inst, Seattle, WA
References Pincus & McClure 1993

- 41.4: Binds to peptide weakly, but to gp160 with higher affinity than 41.1, and cross-competes with 41.1 – probably conformational – MAb was coupled to ricin A chain (RAC) – sCD4 enhances the efficacy of immunotoxins *in vitro* 30-fold. Pincus & McClure [1993]

No. 660
MAb ID Fab A1 (A1)
HXB2 Location gp160 (579–608)
Author Location gp41 (584–609 LAI)
Epitope RILAVERYLKDQQLLGIWGCSGKLICTTAV
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords anti-idiotype, antibody generation, antibody sequence, variable domain, review

- Fab A1: Called A1. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- Fab A1: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**anti-idiotype**, **antibody generation**, **antibody sequence, variable domain**)

No. 661
MAb ID Fab A4 (A4)
HXB2 Location gp160 (579–608)
Author Location gp41 (584–609 LAI)
Epitope RILAVERYLKDQQLLGIWGCSGKLICTTAV
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab A4: Called A4. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- Fab A4: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 662
MAb ID Fab M12B (M12B)
HXB2 Location gp160 (579–608)
Author Location gp41 (584–609 LAI)
Epitope RILAVERYLKDQQLLGIWGCSGKLICTTAV
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab M12B: Called M12B. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- Fab M12B: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 663
MAb ID Fab M26B (M26B)
HXB2 Location gp160 (579–608)
Author Location gp41 (584–609 LAI)
Epitope RILAVERYLKDQQLLGIWGCSGKLICTTAV
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab M26B: Called M26B. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- Fab M26B: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 664
MAb ID Fab M8B (M8B)
HXB2 Location gp160 (579–608)
Author Location gp41 (584–609 LAI)
Epitope RILAVERYLKDQQLLGIWGCSGKLICTTAV
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab M8B: Called M8B. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- Fab M8B: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 665
MAb ID Fab T2 (T2)
HXB2 Location gp160 (579–608)
Author Location gp41 (584–609 LAI)
Epitope RILAVERYLKDQQLLGIWGCSGKLICTTAV
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab T2: Called T2. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- Fab T2: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 666
MAb ID 86 (No. 86)
HXB2 Location gp160 (579–613)
Author Location gp41 (586–620 IIIB)
Epitope RILAVERYLKDQQLLGIWGCSGKLICTTAVPWNAS
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Research Contact Evan Hersh and Yoh-Ichi Matsumoto
References Gorny & Zolla-Pazner 2004; Mitchell *et al.* 1998; Wisnewski *et al.* 1996; Moran *et al.* 1993; Pincus *et al.* 1991; Robinson *et al.* 1990c; Robinson *et al.* 1990b; Sugano *et al.* 1988
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, complement, enhancing activity, immunotoxin, review, variant cross-recognition or cross-neutralization

- 86: NIH AIDS Research and Reference Reagent Program: 380.

- 86: This is one of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 86: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613. Mitchell *et al.* [1998] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- 86: 86 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- 86: Heavy (V HI) and light (V kappaI) chain sequenced – enhancing activity – similar germline sequence to MAb S1-1, but very different activity. Moran *et al.* [1993] (**enhancing activity**, **antibody sequence, variable domain**)
- 86: Poor immunotoxin activity when coupled to RAC – peptide binding stated to be aa 579-603. Pincus *et al.* [1991] (**antibody binding site definition and exposure**, **immunotoxin**)
- 86: Antibody dependent enhancement (ADE) of HIV-1 IIIB infectivity in the presence of complement. Robinson *et al.* [1990b] (**complement**, **enhancing activity**)
- 86: Peptide 586-620 blocks complement mediated ADE. Robinson *et al.* [1990c] (**enhancing activity**)
- 86: Reacts with gp41 and also reacted weakly with gp120. Sugano *et al.* [1988] (**antibody binding site definition and exposure**)

No. 667
MAb ID polyclonal
HXB2 Location gp160 (580–597)
Author Location gp41 (584–602)
Epitope ILAVERYLKDQQLLGIWG
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human
References Petrov *et al.* 1990

- Immunodominant and broadly reactive peptide. Petrov *et al.* [1990]

No. 668
MAb ID V10-9
HXB2 Location gp160 (580–613)
Author Location gp41 (586–620 IIIB)
Epitope ILAVERYLKDQQLLGIWGCSGKLICTTAVPWNAS
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Gorny & Zolla-Pazner 2004; Robinson *et al.* 1990c; Robinson *et al.* 1990b
Keywords antibody interactions, enhancing activity, review

- V10-9: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- V10-9: Antibody dependent enhancement (ADE) of HIV-1 IIIB infectivity, synergistically enhanced by MAb 120-16. Robinson *et al.* [1990b] (**antibody interactions**, **enhancing activity**)
- V10-9: Peptide 586-620 blocks complement mediated ADE. Robinson *et al.* [1990c] (**enhancing activity**)

No. 669
MAb ID polyclonal
HXB2 Location gp160 (582–589)
Author Location gp41 (589–596)
Epitope AVERYLKD
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Klasse *et al.* 1991

- Substitutions and deletions in peptide 583-599 were systematically studied – alterations in AVERYLKD abrogated the antigenicity of peptides with most of 14 human sera. Klasse *et al.* [1991]

No. 670
MAb ID polyclonal
HXB2 Location gp160 (584–604)
Author Location gp41 (74–94)
Epitope ERYLKDQLLGIWGCSGKLIC
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Shafferman *et al.* 1989

- Immunogenic domain useful for diagnostics. Shafferman *et al.* [1989]

No. 671
MAb ID polyclonal
HXB2 Location gp160 (584–612)
Author Location gp41 (587–617 BRU)
Epitope ERYLKDQQLLGIWGCSGKLICTTAVPWNA
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human
References Hernandez *et al.* 2000

- Chimeric peptide combining two peptides gp160(495-516 and 584-612) served as a specific and broadly reactive antigen for diagnostic detection of HIV-1. Hernandez *et al.* [2000]

No. 672
MAb ID 2F11
HXB2 Location gp160 (589–600)
Author Location gp41 (589–600 HXB2)
Epitope DQQLLGIWGCSG
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
References Gorny & Zolla-Pazner 2004; Enshell-Seijffers *et al.* 2001; Eaton *et al.* 1994
Keywords ADCC, enhancing activity, review

- 2F11: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 2F11: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial. Enshell-Seijffers *et al.* [2001] (**enhancing activity**)
- 2F11: Enhances infectivity even in the absence of complement – does not mediate ADCC or neutralize virus. Eaton *et al.* [1994] (**ADCC**, **enhancing activity**)

No. 673
MAb ID 246-D (SZ-246.D, 246, 246D)
HXB2 Location gp160 (590–597)
Author Location gp41 (579–604 HXB2)
Epitope qqLLGIWg
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster I
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Ling *et al.* 2004; Gorny & Zolla-Pazner 2004; Finnegan *et al.* 2002; Follis *et al.* 2002; Edwards *et al.* 2002; Gorny *et al.* 2002; Verrier *et al.* 2001; Nyambi *et al.* 2000; Gorny & Zolla-Pazner 2000; Mitchell *et al.* 1998; Hioe *et al.* 1997b; Earl *et al.* 1997; Saarloos *et al.* 1995; Manca *et al.* 1995a; Forthal *et al.* 1995; Eddleston *et al.* 1993; Spear *et al.* 1993; Robinson *et al.* 1991; Xu *et al.* 1991
Keywords antibody binding site definition and exposure, antibody interactions, complement, enhancing activity, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization

- 246-D: NIH AIDS Research and Reference Reagent Program: 1245.
- 246-D: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 246-D: Called 246D. The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of 17b and F105 was decreased by trypsin, but increased by thrombin. gp41 MAbs 246D, 98.6, 50-69, were decreased by trypsin, unaltered by thrombin, while NAb 2F5 binding was increased by thrombin. Thrombin may increase HIV-induced cell fusion in blood by causing a conformational activating shift in gp120. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 246-D: Called 246D – Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. Edwards *et al.* [2002] (**antibody binding site definition and exposure**)
- 246-D: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. Finnegan *et al.* [2002] (**antibody binding site definition and exposure**, **kinetics**)
- 246-D: Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. Follis *et al.* [2002] (**antibody binding site definition and exposure**)
- 246-D: Called 246 – Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions and the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), and MAb 246 (anti-gp41 MAb that bound to

primary isolates of all clades tested, A, B, C, D, F and CRF01 (clade E) Gorny *et al.* [2002] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

- 246-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001] (**antibody interactions**)
- 246-D: Core epitope aa 591 to 597, a cluster I epitope that does not bind to either a peptide complex that approximates the core of the fusogenic form of gp41 or the individual peptides N51 and C43 that form this structure – MAbs 181-D and 246-D had similar properties. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**)
- 246-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 246-D bound strongly or moderately to all 26 HIV-1 group M clades viruses tested and showed the strongest binding of all anti-Env MAbs tested, including the V3 and C5 region MAbs – notes core epitope as LLGI – no neutralizing activity was observed when 246-D was tested with five isolates. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 246-D: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613. Mitchell *et al.* [1998] (**antibody binding site definition and exposure**)
- 246-D: This antibody, along with murine MAb D61, can be blocked by any of a group of 8 conformational MAbs (M10, D41, D54, T4, T6, T9, T10 and T35) Earl *et al.* [1997] (**antibody interactions**)
- 246-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations and 246-D neutralized 91US056 – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 246-D: No neutralizing activity, both ADCC and viral enhancing activity. Forthal *et al.* [1995] (**complement**, **enhancing activity**)
- 246-D: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells. Manca *et al.* [1995a]
- 246-D: Ab-mediated activation of complement on HIV+ cells is higher than Ab independent activation—what has been termed "Ab independent" in fact results in part from IgM in normal human serum that is HIV-cross-reactive. Saarloos *et al.* [1995] (**complement**)
- 246-D: Called SZ-246.D. Eddleston *et al.* [1993]
- 246-D: Did not mediate deposition of complement component C3 on HIV infected cells unless cells were pre-incubated with sCD4. Spear *et al.* [1993] (**complement**)
- 246-D: No neutralizing activity, some enhancing activity. Robinson *et al.* [1991] (**enhancing activity**)
- 246-D: Fine mapping indicates core is LLGI. Xu *et al.* [1991] (**antibody binding site definition and exposure**)

No. 674
MAb ID polyclonal
HXB2 Location gp160 (590–607)
Author Location gp41
Epitope QQLLGIWGCSGKLICTTA
Subtype B, CRF01_AE
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Parekh *et al.* 2002

- A simple enzyme immunoassay (EIA) that detects increasing levels of anti-HIV IgG after seroconversion can be used for detecting recent HIV-1 infection – longitudinal specimens from 139 incident infections in the US and Thailand were used in the study – the method was generally applicable for HIV-1 subtypes A, B, C, D and E(CRF01) Parekh *et al.* [2002]

No. 675
MAb ID 9G5A
HXB2 Location gp160 (591–594)
Author Location gp41 (596–599 IIIB)
Epitope QLLG
Neutralizing
Immunogen anti-idiotype
Species (Isotype) mouse (IgM)
References Beretta & Dalgleish 1994; Lopalco *et al.* 1993

- 9G5A: Anti-idiotype to gp120 C terminus (C5 region) MAb M38. Lopalco *et al.* [1993]

No. 676
MAb ID 181-D (SZ-181.D)
HXB2 Location gp160 (591–597)
Author Location gp41 (591–597 HXB2)
Epitope qLLGIWg
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG2κ)
Ab Type cluster I
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY
References Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Gorny & Zolla-Pazner 2000; Fontenot *et al.* 1995; Forthal *et al.* 1995; Eddleston *et al.* 1993; Robinson *et al.* 1991; Xu *et al.* 1991

Keywords ADCC, antibody binding site definition and exposure, enhancing activity, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 181-D: This is one of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 181-D: Core epitope aa 591 to 597, a cluster I epitope that does not bind to either a peptide complex that approximates the core of the fusogenic form of gp41 or the individual peptides N51 and C43 that form this structure – MAbs 181-D and 246-D had similar properties. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**)
- 181-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 181-D bound the majority of isolates although binding was moderate to weak. Nyambi *et al.* [2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 181-D: No neutralizing, no ADCC, and no viral enhancing activity. Forthal *et al.* [1995] (**ADCC**, **enhancing activity**)
- 181-D: Called SZ-181.D. Eddleston *et al.* [1993]
- 181-D: No enhancing or neutralization activity. Robinson *et al.* [1991] (**enhancing activity**)
- 181-D: Fine mapping indicates core is LLGIW. Xu *et al.* [1991] (**antibody binding site definition and exposure**)

No. 677
MAb ID 240-D (F240)
HXB2 Location gp160 (592–600)
Author Location gp41 (592–600 HXB2)
Epitope LLGIWGCSG
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type cluster I
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY
References Gorny & Zolla-Pazner 2004; Finnegan *et al.* 2002; Nyambi *et al.* 2000; Mitchell *et al.* 1998; Wisnewski *et al.* 1996; Wisnewski *et al.* 1995; Binley *et al.* 1996; Spear *et al.* 1993; Robinson *et al.* 1991; Xu *et al.* 1991
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, complement, enhancing activity, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization

- 240-D: NIH AIDS Research and Reference Reagent Program: 1242.
- 240-D: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 240-D: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. Finnegan *et al.* [2002] (**antibody binding site definition and exposure**, **kinetics**)
- 240-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 246-D bound strongly or moderately to 24/26 HIV-1 group M clades viruses tested. Nyambi *et al.* [2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 240-D: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613. Mitchell *et al.* [1998] (**enhancing activity**)
- 240-D: Binds to a linear epitope located in the cluster I region – binding of 50-69 and 240-D inhibited by Fabs A1, A4, M8B, M26B, M12B and T2. Binley *et al.* [1996] (**antibody binding site definition and exposure**)
- 240-D: V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- 240-D: Did not mediate deposition of complement component C3 on HIV infected cells. Spear *et al.* [1993] (**complement**)
- 240-D: No neutralizing activity, some enhancing activity. Robinson *et al.* [1991] (**enhancing activity**)
- 240-D: Fine mapping indicates core is IWG. Xu *et al.* [1991] (**antibody binding site definition and exposure**)

No. 678
MAb ID F240
HXB2 Location gp160 (592–606)
Author Location gp41 (592–606 BH10)
Epitope LLGIWGCSGKLICTT
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster I
Research Contact L. Cavacina or M. Posner, Dept. of Med. Harvard Med. School, Boston MA, USA
References Gorny & Zolla-Pazner 2004; Finnegan *et al.* 2002; Follis *et al.* 2002; Cavacini *et al.* 2003; Cavacini *et al.* 2002; York *et al.* 2001; Cavacini *et al.* 1998a

Keywords antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, co-receptor, enhancing activity, review, variant cross-recognition or cross-neutralization

- F240: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- F240: The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. Anti-gp41 MAb F240 could inhibit B4e8 neutralization. Cavacini *et al.* [2003] (**antibody interactions**)
- F240: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate, with the exception of F240 which bound both equally well, which captured more virus than any other human MAb tested, and didn't neutralize either isolate.F240 enhanced the binding of CD4BS MAbs IgG1b12 and F105 and the gp41 MAb 2F5 for both R5X4 and R5 isolates. F240 binding to gp41 was not affected by the binding of the V3 loop MAb B4a1, but preincubation with F240 could enhance B4a1 binding of the R5 isolate. Synergistic neutralization between F240 and CD4i MAbs 17b and 48d was noted for the R5X4 but not the R5 isolate, and F240 also enhanced neutralization of the R5X4 isolate by 2F5, but had no effect on R5 virus. In contrast, F240 combined with 2G12 demonstrated enhanced neutralization of R5 virus at low Ab concentrations. Cavacini *et al.* [2002] (**antibody interactions**, **co-receptor**)
- F240: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. Finnegan *et al.* [2002] (**antibody binding site definition and exposure**)
- F240: Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. Follis *et al.* [2002] (**antibody binding site definition and exposure**)
- F240: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. York *et al.* [2001] (**variant cross-recognition or cross-neutralization**)
- F240: Distinct from MAb 240-D, an antibody with a similar epitope in the immunodominant region of gp41 – dose-dependent reactivity with HIV isolates RF, SF2, IIIB, and MN was observed – F240 had no neutralizing activity and enhances infection in the presence of complement – reactivity of F240 is enhanced by preincubation of cells with sCD4 or anti-CD4BS MAb F105 – heavy and light chain variable domains were sequenced, and a strong homology to hu MAb 3D6 was observed, as 3D6 binds to the same epitope, these MAbs may define a human Ab clonotype. Cavacini *et al.* [1998a] (**enhancing activity**, **variant cross-recognition or cross-neutralization**, **antibody sequence, variable domain**)

No. 679
MAb ID D49
HXB2 Location gp160 (592–608)
Author Location gp41 (597–613)
Epitope LLGIWGCSGKLICTTAV
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* dimeric Env
Species (Isotype) mouse
Ab Type cluster I
References Earl *et al.* 1997; Earl *et al.* 1994

- D49: Binding maps to region 597-613: WGCSGKLICTTAVP-WNA – immunodominant region containing two Cys residues. Earl *et al.* [1997]
- D49: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 680
MAb ID D61
HXB2 Location gp160 (592–608)
Author Location gp41 (592–608 HXB2)
Epitope LLGIWGCSGKLICTTAV
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* dimeric Env
Species (Isotype) mouse

Ab Type cluster I
Research Contact Patricia Earl and Christopher Broder, NIH
References Golding *et al.* 2002b; Earl *et al.* 1997; Weissenhorn *et al.* 1996; Richardson *et al.* 1996; Earl *et al.* 1994
Keywords antibody binding site definition and exposure, antibody generation

- D61: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b – nor did it alter two gp41 MAbs, T9 and D61, inability to inhibit fusion. Golding *et al.* [2002b] (**antibody binding site definition and exposure**)
- D61: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues – this antibody, along with human MAb 246-D, can be blocked by any of a group of 8 conformational MAbs (M10, D41, D54, T4, T6, T9, T10 and T35) – members of this competition group are blocked by sera from HIV-1 + individuals. Earl *et al.* [1997] (**antibody binding site definition and exposure**)
- D61: Linear gp41 epitope in the cluster I region – human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4. Richardson *et al.* [1996] (**antibody binding site definition and exposure**)
- D61: Does not precipitate gp41(21-166), but due to a structural difference in the disulfide bonding region near the two cysteines – the authors propose that this region may change conformation during the activation of the membrane fusion state of the HIV-1 glycoprotein. Weissenhorn *et al.* [1996] (**antibody binding site definition and exposure**)
- D61: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994] (**antibody generation**)

No. 681
MAb ID T32
HXB2 Location gp160 (592–608)
Author Location gp41 (597–613)
Epitope LLGIWGCSGKLICTTAV
Neutralizing
Immunogen Vaccine
Vector/Type: tetrameric Env *HIV component:* Env
Species (Isotype) mouse
Ab Type cluster I
Research Contact Patricia Earl and Christopher Broder, NIH
References Earl *et al.* 1997; Earl *et al.* 1994

- T32: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues. Earl *et al.* [1997]
- T32: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 682
MAb ID T34
HXB2 Location gp160 (592–608)
Author Location gp41 (597–613)
Epitope LLGIWGCSGKLICTTAV
Neutralizing
Immunogen Vaccine
Vector/Type: tetrameric Env *HIV component:* Env
Species (Isotype) mouse
Ab Type cluster I
Research Contact Patricia Earl and Christopher Broder, NIH
References Earl *et al.* 1997; Earl *et al.* 1994

- T34: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues. Earl *et al.* [1997]
- T34: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response – an oligomer with no gp120/gp41 cleavage site was used as the immunogen. Earl *et al.* [1994]

No. 683
MAb ID 115.8
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGLIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgM)
References Oldstone *et al.* 1991

- 115.8: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor reactivity with CSGKLIC – reacts well with longer HIV-2 peptide NSWGCAFRQVC as well as CAFRQVC – disulfide bond between cysteines required. Oldstone *et al.* [1991]

No. 684
MAb ID M-1
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG1, IgG2b)
References Yamada *et al.* 1991

- M-1: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. Yamada *et al.* [1991]

No. 685
MAb ID M-11
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG1)
References Yamada *et al.* 1991

- M-11: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. Yamada *et al.* [1991]

No. 686
MAb ID M-13
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG2b)
References Yamada *et al.* 1991

- M-13: Reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. Yamada *et al.* [1991]

No. 687
MAb ID M-2
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG2b)
References Yamada *et al.* 1991

- M-2: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. Yamada *et al.* [1991]

No. 688
MAb ID M-22
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG2b)
References Yamada *et al.* 1991

- M-22: Strongest reaction of 12 anti-HIV-1 gp41 MAbs to a cellular 43-kd protein found in rat and human astrocytes. Yamada *et al.* [1991]

No. 689
MAb ID M-24
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG1)
References Yamada *et al.* 1991

- M-24: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. Yamada *et al.* [1991]

No. 690
MAb ID M-25
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG1)
References Yamada *et al.* 1991

- M-25: Reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. Yamada *et al.* [1991]

No. 691
MAb ID M-28
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG1)
References Yamada *et al.* 1991

- M-28: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. Yamada *et al.* [1991]

No. 692
MAb ID M-29
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG1)
References Yamada *et al.* 1991

- M-29: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. Yamada *et al.* [1991]

No. 693
MAb ID M-36
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG1)
References Yamada *et al.* 1991

- M-36: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. Yamada *et al.* [1991]

No. 694
MAb ID M-4
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41

Species (Isotype) mouse (IgG2b)
References Yamada *et al.* 1991

- M-4: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. Yamada *et al.* [1991]

No. 695
MAb ID M-6
HXB2 Location gp160 (593–604)
Author Location gp41 (598–609)
Epitope LGIWGCSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG2b)
References Yamada *et al.* 1991

- M-6: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. Yamada *et al.* [1991]

No. 696
MAb ID polyclonal α598-609
HXB2 Location gp160 (594–601)
Author Location gp41 (598–609)
Epitope GIWGCSGK
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Poumbourios *et al.* 1992

- alpha(598-609): Affinity purified from HIV-1 + plasma – immunodominant region, binds oligomer and monomer. Poumbourios *et al.* [1992]

No. 697
MAb ID 1B8.env (1B8)
HXB2 Location gp160 (594–604)
Author Location gp41 (594–605 HXB2)
Epitope GIWGCSGKLIC
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG2λ)
References Gorny & Zolla-Pazner 2004; Enshell-Seijffers *et al.* 2001; Banapour *et al.* 1987
Keywords antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization

- 1B8B.env: Called 1B8. There are 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 1B8.env: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial. Enshell-Seijffers *et al.* [2001]
- 1B8.env: Highly conserved epitope recognized by the majority of HIV-1 infected people – MAb does not neutralize. Banapour *et al.* [1987] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

No. 698
MAb ID polyclonal
HXB2 Location gp160 (594–609)
Author Location gp41 (601–616)
Epitope GIWGCSGKLICTTAVP
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human
References Petrov *et al.* 1990

- Immunodominant and broadly reactive peptide. Petrov *et al.* [1990]

No. 699
MAb ID polyclonal
HXB2 Location gp160 (595–607)
Author Location gp41 (600–612)
Epitope IWGCSGKLICTTA
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Belliard *et al.* 2003
Country France
Keywords rate of progression

- Sera from 101 slow progressors and 42 fast progressors were tested for responses to Tat peptides, and compared to responses to gp41 peptide 600-612, as anti-Tat antibodies had been shown by others to be elevated in slow progressors. Most patient sera react with this peptide, it is used in diagnostics. In this study, overall levels of Tat antibodies were not different in the two groups, however relative levels of antibodies to different Tat peptides and to this gp41 peptide were observed. Belliard *et al.* [2003] (**rate of progression**)

No. 700
MAb ID clone 3
HXB2 Location gp160 (597–606)
Author Location gp41 (597–606)
Epitope GCSGKLICTT
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
References Gorny & Zolla-Pazner 2004; Enshell-Seijffers *et al.* 2001; Cotropia *et al.* 1996; Cotropia *et al.* 1992; Broliden *et al.* 1989
Keywords antibody binding site definition and exposure, inter-clade comparisons, rate of progression, responses in children, review, variant cross-recognition or cross-neutralization

- clone 3: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. clone 3 neutralized 3 diverse B clade TCLA strains and 3 primary O group strains. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**)
- clone 3: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial. Enshell-Seijffers *et al.* [2001] (**variant cross-recognition or cross-neutralization**)

- clone 3: Inhibits replication of three diverse HIV-1 laboratory strains, as well as an AZT-resistant isolate. Cotropia *et al.* [1996] (**variant cross-recognition or cross-neutralization**)
- clone 3: Core binding domain gcsgkLIC – lack of serological activity to this region correlates with rapid progression in infants (Broliden *et al.* [1989]) Cotropia *et al.* [1992]. Broliden *et al.* [1989]; Cotropia *et al.* [1992] (**antibody binding site definition and exposure**, **responses in children**, **rate of progression**)

No. 701
MAb ID 4
HXB2 Location gp160 (598–604)
Author Location gp41 (598–609)
Epitope CSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG2b)
References Bizub-Bender *et al.* 1994; Oldstone *et al.* 1991

- There is another MAb with this ID that reacts with integrase. Bizub-Bender *et al.* [1994]; Oldstone *et al.* [1991]
- 4: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor cross-reactivity with HIV-2 peptide CAFRQVC – slightly more reactive with longer HIV-2 peptide NSWGCAFRQVC. Oldstone *et al.* [1991]

No. 702
MAb ID 41-6
HXB2 Location gp160 (598–604)
Author Location gp41 (598–609)
Epitope CSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgG2b)
References Oldstone *et al.* 1991

- 41-6: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor cross-reactivity with HIV-2 peptide CAFRQVC – slightly more reactive with LGLIWGCSGKLIC and HIV-2 form NSWGCAFRQVC – disulfide bond between cysteines required. Oldstone *et al.* [1991]

No. 703
MAb ID 41-7
HXB2 Location gp160 (598–604)
Author Location gp41 (605–611)
Epitope CSGKLIC
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Enshell-Seijffers *et al.* 2001; Bugge *et al.* 1990

- 41-7: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial. Enshell-Seijffers *et al.* [2001]
- 41-7: Sera from 6/6 HIV-1 positive, but no HIV-2 positive individuals, interfered with 41-7 binding – Ab does not neutralize. Bugge *et al.* [1990]

No. 704
MAb ID 68.1
HXB2 Location gp160 (598–604)
Author Location gp41 (598–609)
Epitope CSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgM)
References Oldstone *et al.* 1991

- 68.1: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – cross-reactive with HIV-2 peptide CAFRQVC – more reactive with longer HIV-1 peptide LGLIWGCSGKLIC and HIV-2 peptide NSWGCAFRQVC. Oldstone *et al.* [1991]

No. 705
MAb ID 68.11
HXB2 Location gp160 (598–604)
Author Location gp41 (598–609)
Epitope CSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) mouse (IgM)
References Oldstone *et al.* 1991

- 68.11: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – cross-reactive with HIV-2 peptide CAFRQVC – more reactive with longer HIV-1 peptide LGLIWGCSGKLIC and HIV-2 peptide NSWGCAFRQVC. Oldstone *et al.* [1991]

No. 706
MAb ID 75
HXB2 Location gp160 (598–604)
Author Location gp41 (598–609)
Epitope CSGKLIC
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) rat (IgG)
References Oldstone *et al.* 1991

- 75: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor cross-reactivity with HIV-2 peptide CAFRQVC – more reactive with longer HIV-2 peptide NSWGCAFRQVC. Oldstone *et al.* [1991]

No. 707
MAb ID polyclonal
HXB2 Location gp160 (598–604)
Author Location gp41 (603–609)
Epitope CSGKLIC
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Enshell-Seijffers *et al.* 2001

- Monoclonal antibodies to this epitope have distinct phenotypes – 41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial – isolated mimotope-presenting phages corresponding to the immunodominant gp41 epitope CSGKLIC were used to study the diversity of polyclonal responses in 30 HIV+ sera, and all but one of the patients reacted showing distinctive variable polyclonal recognition patterns. Enshell-Seijffers *et al.* [2001]

No. 708
MAb ID 105-732
HXB2 Location gp160 (599–606)
Author Location gp41 (601–608 HAM112, O group)
Epitope KGRLICYT
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* O group HAM112 *HIV component:* gp160
Species (Isotype) mouse (IgG2bκ)
References Scheffel *et al.* 1999

- 105-732: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – MAb 105-732 bound to two overlapping peptides. Scheffel *et al.* [1999]

No. 709
MAb ID 3D6 (IAM 41-3D6)
HXB2 Location gp160 (599–613)
Author Location gp41 (604–617 BH10)
Epitope SGKLICTTAVPWNAS
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster I, immunodominant region
Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria and Viral Testing Systems, Houston, TX
References Gorny & Zolla-Pazner 2004; Finnegan *et al.* 2002; Cavacini *et al.* 1999; Cavacini *et al.* 1998a; Cavacini *et al.* 1998b; Kunert *et al.* 1998; Wisnewski *et al.* 1996; Stigler *et al.* 1995; Sattentau *et al.* 1995; Chen *et al.* 1994b; He *et al.* 1992; Felgenhauer *et al.* 1990
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, kinetics, review, structure

- 3D6: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 3D6: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. Finnegan *et al.* [2002] (**antibody binding site definition and exposure**, **kinetics**)
- 3D6: Cavacini *et al.* note that both MAbs F223 and 3D6 are anti-HIV-1 Env MAbs that have an autoimmune response and that both use uses VH3 germline genes. Cavacini *et al.* [1999]
- 3D6: Binds to the immunodominant region of gp41 – a strong homology between heavy variable domains of hu MAb 3D6 and MAb F20 was observed, these MAbs may define a human Ab clonotype. Cavacini *et al.* [1998a] (**antibody sequence, variable domain**)
- 3D6: The complete V, J and D(H) domain was sequenced – in contrast the sequences of five neutralizing MAbs, 3D6 had very little somatic mutation, with homologies of 97-98% relative to germline genes. Kunert *et al.* [1998] (**antibody sequence, variable domain**)
- 3D6: 3D6 is V H3 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- 3D6: Called IAM 41-3D6: binding increased after pretreatment of infected cells with sCD4 – binding domain overlaps site that is critical for gp120-gp41 association. Sattentau *et al.* [1995] (**antibody binding site definition and exposure**)
- 3D6: Optimum peptide for binding 3D6 Fab was CSGKLICTTAVPW. Stigler *et al.* [1995] (**antibody binding site definition and exposure**)
- 3D6: This MAb binds to HIV gp41, and to a 43 kd protein found in human T, B and monocyte cell lines, proposed molecular mimicry. Chen *et al.* [1994b]
- 3D6: Fab fragment crystal structure. He *et al.* [1992] (**structure**)
- 3D6: Sequence of cDNA encoding V-regions. Felgenhauer *et al.* [1990] (**antibody sequence, variable domain**)

No. 710
MAb ID F172-D8 (F172-D8, scFvD8)
HXB2 Location gp160 (604–615)
Author Location gp41 (609–620)
Epitope CTTAVPWNASWS?
Neutralizing
Immunogen
Species (Isotype) human
References Legastelois & Desgranges 2000

- F172-D8: As an approach to intercellular immunization using a single-chain variable fragment, scFvD8 was constructed based on the MAb F172-D8, directed at a loop in gp41 between the two heptad repeat regions – intracellular scFvD8 expression decreased gp160 expression and a scFvD8 transfected cell line did not support infection by HIV-1 Ba-L or primary isolates. Legastelois & Desgranges [2000]

No. 711
MAb ID 5-21-3
HXB2 Location gp160 (642–665)
Author Location gp41 (642–665 HXB2)
Epitope IHSLIEESQNQQEKNEQELLELDK
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp41
Species (Isotype) mouse
References Scheffel *et al.* 1999; Hunt *et al.* 1990

- 5-21-3: Binds group M gp41, used as a control in a study of group O MAbs. Scheffel *et al.* [1999]
- 5-21-3: Recognizes a contiguous, conformation-dependent epitope in a hydrophilic region. Hunt *et al.* [1990]

No. 712
MAb ID 120-16 (SZ-120.16)
HXB2 Location gp160 (644–663)
Author Location gp41 (644–663 HXB2)
Epitope SLIEESQNQQEKNEQELLEL
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG2κ)
References Wisnewski *et al.* 1996; Forthal *et al.* 1995; Eddleston *et al.* 1993; Robinson *et al.* 1991; Xu *et al.* 1991; Tyler *et al.* 1990; Robinson *et al.* 1990b; Andris *et al.* 1992

- 120-16: 120-16 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996]
- 120-16: No neutralizing activity, both ADCC and viral enhancing activity. Forthal *et al.* [1995]
- 120-16: Called SZ-120.16. Eddleston *et al.* [1993]
- 120-16: Synergizes with huMAb 50-69 *in vitro* to enhance HIV-1 infection. Robinson *et al.* [1991]
- 120-16: Less reactive region than AVERY region – most Abs involving this region bound conformational epitopes, this was the only linear one. Xu *et al.* [1991]
- 120-16: Antibody dependent enhancement (ADE) of HIV-1 IIIB infectivity, synergistically enhanced by MAb V10-9. Robinson *et al.* [1990b]
- 120-16: Potent ADCC (in contrast to MAb 98-43, gp41(579-604)) Tyler *et al.* [1990]

No. 713
MAb ID 98-6 (SZ-98.6, 98.6, 98-6D)
HXB2 Location gp160 (644–663)
Author Location gp41 (644–663 HXB2)
Epitope SLIEESQNQQEKNEQELLEL
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG2κ)
Ab Type alpha-helical hairpin intermediate, cluster II
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY
References Ling *et al.* 2004; Gorny & Zolla-Pazner 2004; Finnegan *et al.* 2002; Follis *et al.* 2002; Golding *et al.* 2002b; Verrier *et al.* 2001; Taniguchi *et al.* 2000; Nyambi *et al.* 2000; Gorny *et al.* 2000; Gorny & Zolla-Pazner 2000; Nyambi *et al.* 1998; Hioe *et al.* 1997b; Wisnewski *et al.* 1996; Sattentau *et al.* 1995; Manca *et al.* 1995a; Forthal *et al.* 1995; Chen *et al.* 1995; Laal *et al.* 1994; Tani *et al.* 1994; Spear *et al.* 1993; Eddleston *et al.* 1993; Xu *et al.* 1991; Robinson *et al.* 1991; Sattentau & Moore 1991; Andris *et al.* 1992; Tyler *et al.* 1990; Robinson *et al.* 1990b; Till *et al.* 1989; Gorny *et al.* 1989; Pinter *et al.* 1989
Keywords ADCC, antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, binding affinity, complement, enhancing activity, immunotoxin, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization

- 98-6: NIH AIDS Research and Reference Reagent Program: 1240.
- 98-6: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have any neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- 98-6: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of 17b and F105 was decreased by trypsin, but increased by thrombin. gp41 MAbs 246D, 98.6, 50-69, were decreased by trypsin, unaltered by thrombin, while NAb 2F5 binding was increased by thrombin. Thrombin may increase HIV-induced cell fusion in blood by causing a conformational activating shift in gp120. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 98-6: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing.

These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. Finnegan *et al.* [2002] (**antibody binding site definition and exposure**, **kinetics**)

- 98-6: Called 98-6D. Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. Follis *et al.* [2002] (**antibody binding site definition and exposure**)
- 98-6: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – 98-6 binds to a C-HR hairpin epitope and blocks fusion when added to a 2 hour E/T preincubation at 31.5 C, but if added after 1 hour, doesn't inhibit – this is in contrast to six-helix bundle Abs 167-D and 1281 that inhibit more efficiently when added after one hour of incubation. Golding *et al.* [2002b] (**antibody binding site definition and exposure**)
- 98-6: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6—six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D, while six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 98-6: 98-6 and 2F5 both bind to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, and to C43 alone but not to N51 alone – 98-6 and 2F5 have comparable affinities for C43, but 98-6 has a higher affinity for the complex and the binding of 98-6 is not inhibited by N51. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**, **binding affinity**)
- 98-6: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)
- 98-6: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs – no neutralizing activity was observed when tested against 5 isolates, but 98-6 did not bind to these isolates. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 98-6: The fusogenic form of gp41 is recognized by 98-6, and the epitope is a conformational epitope formed by the interaction of two regions of gp41 which form an alpha-helical bundle. Taniguchi *et al.* [2000] (**antibody binding site definition and exposure**)
- 98-6: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98-6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade. Nyambi *et al.* [1998] (**variant cross-recognition or cross-neutralization**)
- 98-6: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 98-6: 98-6 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- 98-6: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation. Chen *et al.* [1995] (**antibody binding site definition and exposure**)
- 98-6: No neutralizing activity, positive ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995] (**ADCC**, **enhancing activity**)
- 98-6: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells. Manca *et al.* [1995a]
- 98-6: Preferentially recognizes oligomeric form of gp41 – enhanced binding to HIV-1 infected cells at 37 degrees relative to 4 degrees – addition of sCD4 enhances binding. Sattentau *et al.* [1995] (**antibody binding site definition and exposure**)
- 98-6: Epitope described as cluster II, 644-663, conformational – does not neutralize IIIB or synergize neutralization by anti-V3 MAb 447-52D or by CD4 BS MAbs. Laal *et al.* [1994] (**antibody binding site definition and exposure**, **antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 98-6: This MAb was expressed as a surface anti-gp41 monoclonal antibody receptor for gp41 on a CD4-negative B-cell line. Transfected cells could bind HIV Envelope, but could not be infected by HIV-1. When CD4 delivered by retroviral constructs was expressed on these cells, they acquired the ability to replicate HIV-1, and sIg/gp41 specifically enhanced viral replication. Tani *et al.* [1994]

- 98-6: Called SZ-98.6 – binds to a conformational domain within aa 644-663 of gp41, and reacts with astrocytes, as do 167-7 and ND-15G1. Eddleston *et al.* [1993] (**antibody binding site definition and exposure**)
- 98-6: Did not mediate deposition of complement component C3 on HIV infected cells, binding enhanced by sCD4. Spear *et al.* [1993] (**complement**)
- 98-6: No neutralizing or enhancing activity. Robinson *et al.* [1991] (**enhancing activity**)
- 98-6: Two fold increase in binding to gp120 in the presence of bound sCD4. Sattentau & Moore [1991] (**antibody binding site definition and exposure**)
- 98-6: Appeared to be specific for a conformational or discontinuous epitope. Xu *et al.* [1991] (**antibody binding site definition and exposure**)
- 98-6: No neutralizing or enhancing activity for HIV-1 IIIB. Robinson *et al.* [1990b] (**enhancing activity**)
- 98-6: Serves as target for antibody-dependent cellular cytotoxicity, ADCC. Tyler *et al.* [1990] (**ADCC**)
- 98-6: Kills HIV-infected cells when coupled to deglycosylated ricin A chain. Gorny *et al.* [1989] (**immunotoxin**)
- 98-6: Reacts preferentially with gp160 oligomer, compared to gp41 monomer. Pinter *et al.* [1989] (**antibody binding site definition and exposure**)
- 98-6: Toxic to HIV-infected T cells (H9) and monocytes (U937) when coupled to deglycosylated A chain of ricin. Till *et al.* [1989] (**immunotoxin**)

No. 714
MAb ID 167-7 (SZ-167.7)
HXB2 Location gp160 (644–663)
Author Location gp41 (644–663)
Epitope SLIEESQNQQEKNEQELLEL
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG2λ)
Ab Type cluster II
References Eddleston *et al.* 1993; Xu *et al.* 1991

- 167-7: Called SZ-167.7 – binds to a conformational domain within aa 644-663 of gp41, and reacts with astrocytes, as do 98-6 and ND-15G1. Eddleston *et al.* [1993]
- 167-7: Specific for a conformational epitope. Xu *et al.* [1991]

No. 715
MAb ID ND-15G1 (ND-15GI)
HXB2 Location gp160 (644–663)
Author Location gp41 (644–663 HXB2)
Epitope SLIEESQNQQEKNEQELLEL
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Eddleston *et al.* 1993
Keywords antibody binding site definition and exposure, review

- ND-15G1: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- ND-15G1: Mapped to the conformational epitope within aa 644-663, and reacts with astrocytes, as do 98-6 and 167-7. Eddleston *et al.* [1993] (**antibody binding site definition and exposure**)

No. 716
MAb ID 167-D (167)
HXB2 Location gp160 (644–663)
Author Location gp41 (644–663 HXB2)
Epitope SLIEESQNQQEKNEQELLEL
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type cluster II, six-helix bundle
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY
References Gorny & Zolla-Pazner 2004; Golding *et al.* 2002b; Nyambi *et al.* 2000; Gorny *et al.* 2000; Gorny & Zolla-Pazner 2000; Manca *et al.* 1995a; Forthal *et al.* 1995; Spear *et al.* 1993
Keywords ADCC, antibody binding site definition and exposure, complement, enhancing activity, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 167-D: Called 167. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- 167-D: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – 98-6 binds to a C-HR hairpin epitope and blocks fusion when added to a 2 hour E/T preincubation at 31.5 C, but if added after 1 hour, doesn't inhibit – this is in contrast to six-helix bundle Abs 167-D and 1281 that inhibit more efficiently when added after one hour of incubation. Golding *et al.* [2002b] (**antibody binding site definition and exposure**)
- 167-D: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**)
- 167-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)

- 167-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 167-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995] (**ADCC**, **enhancing activity**, **variant cross-recognition or cross-neutralization**)
- 167-D: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells. Manca *et al.* [1995a]
- 167-D: Did not mediate deposition of complement component C3 on HIV infected cells – complement mediated virolysis of MN and IIIB in the presence of sCD4. Spear *et al.* [1993] (**complement**)

No. 717
MAb ID 2F5 (IAM 2F5, IAM-41-2F5, IAM2F5, c2F5)
HXB2 Location gp160 (656–671)
Author Location gp41 (662–667 BH10)
Epitope NEQELLELDKWASLWN
Neutralizing L P
Immunogen HIV-1 infection
Species (Isotype) human (IgG3κ)
Ab Type adjacent to cluster II, C-term
Research Contact Hermann Katinger, Institute of Applied Microbiology, Vienna, or Polymun Scientific Inc., Vienna, Austria, or Viral Testi
References Menendez *et al.* 2004; Safrit *et al.* 2004; Pugach *et al.* 2004; Pinter *et al.* 2004; Opalka *et al.* 2004; Nabatov *et al.* 2004; McCaffrey *et al.* 2004; Lorin *et al.* 2004; Ling *et al.* 2004; Liao *et al.* 2004; Jeffs *et al.* 2004; de Rosny *et al.* 2004a; de Rosny *et al.* 2004b; Zwick *et al.* 2004; Gorny & Zolla-Pazner 2004; Wolbank *et al.* 2003; Ohagen *et al.* 2003; Montefiori *et al.* 2003; McGaughey *et al.* 2003; Kitabwalla *et al.* 2003; Wang 2003; Richman *et al.* 2003; Mascola 2003; Hart *et al.* 2003; Ferrantelli *et al.* 2003; Dey *et al.* 2003; Binley *et al.* 2003; Stiegler *et al.* 2002; Li *et al.* 2002; Huang *et al.* 2002; Gorry *et al.* 2002; Finnegan *et al.* 2002; Follis *et al.* 2002; Cavacini *et al.* 2002; Bures *et al.* 2002; Liu *et al.* 2002; Ferrantelli & Ruprecht 2002; Zhang *et al.* 2002; Kunert *et al.* 2002; Mascola 2002; Grundner *et al.* 2002; Xiang *et al.* 2002b; Clerici *et al.* 2002a; Joyce *et al.* 2002; Chakrabarti *et al.* 2002; Xu *et al.* 2002; Ho *et al.* 2002; Tian *et al.* 2002; Schulke *et al.* 2002; Golding *et al.* 2002b; Srivastava *et al.* 2002; Armbruster *et al.* 2002; Root *et al.* 2001; Xu *et al.* 2001; Hofmann-Lehmann *et al.* 2001; Stiegler *et al.* 2001; Verrier *et al.* 2001; Spenlehauer *et al.* 2001; Parker *et al.* 2001; Zeder-Lutz *et al.* 2001; Moore *et al.* 2001; Barnett *et al.* 2001; Mascola & Nabel 2001; Zwick *et al.* 2001c; Zwick *et al.* 2001b; York *et al.* 2001; Tumanova *et al.* 2001; Kolchinsky *et al.* 2001; Dong *et al.* 2001; Si *et al.* 2001; Yang *et al.* 2000; Xiao *et al.* 2000c; Coeffier *et al.* 2000; Sanhadji *et al.* 2000; Pai *et al.* 2002; Park *et al.* 2000; Nyambi *et al.* 2000; Lu *et al.* 2000b; Lu *et al.* 2000c; Liao *et al.* 2000; Kunert *et al.* 2000; Gorny & Zolla-Pazner 2000; Robert-Guroff 2000; Baba *et al.* 2000; Mascola *et al.* 2000; Mascola *et al.* 1999; Parren *et al.* 1999; Muhlbacher *et al.* 1999; Beddows *et al.* 1999; Poignard *et al.* 1999; Montefiori & Evans 1999; Frankel *et al.* 1998; Kunert *et al.* 1998; Geffin *et al.* 1998; Parren *et al.* 1998b; Jiang *et al.* 1998; Li *et al.* 1998; Takefman *et al.* 1998; Ernst *et al.* 1998; Fouts *et al.* 1998; Trkola *et al.* 1998; Yang *et al.* 1998; Parren *et al.* 1998a; Connor *et al.* 1998; Mondor *et al.* 1998; Andrus *et al.* 1998; Gorny *et al.* 1997; Earl *et al.* 1997; Burton & Montefiori 1997; Ugolini *et al.* 1997; Turbica *et al.* 1997; Stamatatos *et al.* 1997; Mascola *et al.* 1997; Moore & Trkola 1997; Kessler II *et al.* 1997; Li *et al.* 1997; Mo *et al.* 1997; D'Souza *et al.* 1997; Schutten *et al.* 1997; Purtscher *et al.* 1996; Stoiber *et al.* 1996; McKeating *et al.* 1996; Pincus *et al.* 1996; Conley *et al.* 1996; Sattentau 1996; Poignard *et al.* 1996b; McKeating 1996; Calarota *et al.* 1996; Kessler *et al.* 1995; Neurath *et al.* 1995; Moore & Ho 1995; Sattentau *et al.* 1995; Trkola *et al.* 1995; D'Souza *et al.* 1995; Beretta & Dalgleish 1994; Muster *et al.* 1994; Chen *et al.* 1994b; Thali *et al.* 1994; Conley *et al.* 1994b; D'Souza *et al.* 1994; Buchacher *et al.* 1994; Laal *et al.* 1994; Purtscher *et al.* 1994; Klasse *et al.* 1993a; Allaway *et al.* 1993; Muster *et al.* 1993; Buchacher *et al.* 1992
Keywords antibody binding site definition and exposure, assay standardization/improvement, coreceptor, immunoprophylaxis, mimotopes, mother-to-infant transmission, reversion, viral fitness, vaccine antigen design, variant cross-recognition or cross-neutralization

- 2F5: UK Medical Research Council AIDS reagent: ARP3063.
- 2F5: NIH AIDS Research and Reference Reagent Program: 1475.
- 2F5: This paper reviews MAbs that bind to HIV-1 Env. 2F5 binds to a region of gp41 proximal to cluster II (aa 662-676), neighboring the binding site of the broadly neutralizing MAb 4E10 and of neutralizing Fab Z13. 2F5 is broadly neutralizing. Gorny & Zolla-Pazner [2004]
- 2F5: A set of oligomeric envelope proteins were made from six primary isolates for potenial use as vaccine antigens: 92/UG/037 (clade A), HAN2/2 (clade B), 92/BR25/025 (clade C), 92/UG/021 (clade D), 93/BR/029 (clade F) and MVP5180 (clade O). This was one of a panel of MAbs used to explore folding and exposure of well characterized epitopes. The clade C isolate BR25 is apparently misfolded, as conformation-dependent antibodies did not bind to it. 2F5 bound to clade A, B, D and F HIV-1 primary isolates. Polyclonal sera raised in

rabbits against these antigens cross-bound the other antigens, but none of the sera had neutralizing activity. Jeffs *et al.* [2004]

- 2F5: 2F5 was used as a positive control in a study that showed that A32-rgp120 complexes open up the CCR5 co-receptor binding site, but did not induce neutralizing antibodies with greater breadth among B subtype isolates than did uncomplexed rgp120 in vaccinated guinea pigs. Liao *et al.* [2004]
- 2F5: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of 17b and F105 was decreased by trypsin, but increased by thrombin. gp41 MAbs 246D, 98.6, 50-69, were decreased by trypsin, unaltered by thrombin, while NAb 2F5 binding was increased by thrombin. Thrombin may increase HIV-induced cell fusion in blood by causing a conformational activating shift in gp120. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 2F5: Mice susceptible to MV infection were intraperitoneally immunized with native HIV-1 89.6 env gp160 and gp140 and δV3 HIV-1 89.6 mutants expressed in live attenuated Schwarz measles vector (MV). The gp160ΔV3 construct raised more cross-reactive NAbs to primary isolates. The constructs had an additional 2F5 MAb epitope, ELDKWAS, but responses were not directed towards this epitope. A HIVIG/2F5/2G12 combination was used as a positive control and could neutralize all isolates. Lorin *et al.* [2004] (**vaccine antigen design**)
- 2F5: Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The loss of the glycan within the V3 loop (GM299 V3) and adjacent to the C-terminal end of the V3 loop (GM329 C3) did not alter neutralization susceptibility to 2F5, but the loss of glycans in C2 (GM292 C2), C4 (GM438 C4), or V5 (GM454 V5) increased 2F5 neutralization susceptibility. V3 glycans tended to shield V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans shielded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 2F5: 2F5 was used for screening of phage-displayed peptide libraries. 2F5 requires the DKW core for synthetic and phage-displayed peptide recognition, but is multispecific for amino acid residues flanking C-terminally the DKW core epitope. Three clones from the AADKW-X12 library had high affinity for 2F5, but did not share obvious holomogy with gp41 or each other; Ala substitution showed each bound to 2F5 with a different mechanism. Menendez *et al.* [2004] (**antibody binding site definition and exposure**, **mimotopes**)
- 2F5: A set of HIV-1 chimeras that altered V3 net charge and glycosylation patterns in V1V2 and V3, involving inserting V1V2 loops from a late stage primary isolate taken after the R5 to X4 switch, were studied with regard to phenotype, co-receptor usage, and MAb neutralization. The loops were cloned into a HXB2 envelope with a LAI viral backbone. It was observed that the addition of the late-stage isolate V1V2 region and the loss of V3-linked glycosylation site in the context of high positive charge gave an X4 phenotype. R5X4, R5, and X4 viruses were generated, and sCD4, 2G12 and b12 neutralization resistance patterns were modified by addition of the late stage V1V2, glycosylation changes, and charge in concert, while neutralization by 2F5 was unaffected. Nabatov *et al.* [2004] (**antibody binding site definition and exposure**, **co-receptor**)
- 2F5: An antigen panel representing different regions of gp41 was generated, and sera from 23 individuals were screened. Anti-gp41 titers were very high, and sera bound to many regions of gp41, there were no immunologically silent regions. Many individuals had broad responses to diverse regions. High titer responses tended to focus on the N-heptad, C-heptad and 2F5-4E10 regions, but there was no correlation between neutralization capacity of sera and the particular peptides recognized. 2F5 responded to the four antigens that carried the minimal EDLKWA epitope. 2F5 did not bind to the minimal epitope embedded in an alpha helix, supporting that the 2F5 conformation of EDLKWA is embedded in a beta sheet. 2F5 bound better to a synthetic peptide containing the proximal regions than to the native gp41. Opalka *et al.* [2004] (**assay standardization/improvement**)
- 2F5: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 2F5: A primary isolate, CC1/85, was passaged 19 times in PBMC and gradually acquired increased sensitivity to FAb b12 and sCD4 that was attributed to changes in the V1V2 loop region, in particular the loss of a potential glycosylation site. The affinity for sCD4 was unchanged in the monomer, suggesting that the structural impact of the change was manifested at the level of the trimer. The passaged virus, CCcon19, retained an R5 phenotype and its neutralization susceptibility to other Abs was essentially the same as CC1/85. The IC50 for 2F5 was greater than 50 for CC1/85, and was 35 for CCcon19, so the passaged virus was weakly neutralized by 2F5. Pugach *et al.* [2004] (**reversion, viral fitness**, **variant cross-recognition or cross-neutralization**)
- 2F5: The MAb 2F5 binds to the C-heptad and is neutralizing, but the MAb D50 binds to the C-heptad and is not neutralizing. 2F5 binds preferentially to native gp41 prior to receptor activation. D50 prefers the triggered form after receptor activation. Trapped fusion-intermediates suggest 2F5 remains present shortly after gp120 triggering by CD4, but may be lost by the time the six-helix bundle is formed. D50 binds equally to the fusion-intermediate and six-helix bundle. 2F5 neutralization seems to block a later step of the fusion process, but it does not inhibit binding of NC-1, a MAb specific for the six-helix bundle, so it does not prevent formation of the six-helix

bundle. The results are most consistent with 2F5 inhibiting a post-fusion-intermediate step. de Rosny *et al.* [2004b]

- 2F5: The mechanism of 2F5 neutralization was explored, and experiments suggest it is due to interference with a late step in viral entry. sCD4 binding to gp120 triggers conformational changes in gp41 allowing formation of the six helix bundle. The NAb 2F5 preferentially bound native gp41, prior to receptor triggering, while the antibody D50 that also binds to the heptad region, near 2F5, is not neutralizing, and preferentially bound the CD4-triggered gp41. The C and N peptides that can be used to block the formation of the six helix bundle and lock gp41 in the fusion intermediate state after sCD4 triggering enabled 2F5 to bind after sCD4, while D50 was able to bind to both the peptide-trapped and sCD4 induced six helix bundle equally well. The peptide-trapping studies suggest that 2F5 does not fix Env in the native conformation, but interferes with entry after the initial conformation changes occur. Nor does it block six-helix bundle formation, as 2F5 prebinding does not inhibit NC-1 binding, a MAb that binds specifically to the six-helix bundle. de Rosny *et al.* [2004a]
- 2F5: This review discusses research presented at the Ghent Workshop of prevention of breast milk transmission and immunoprophylaxis for HIV-1 in pediatrics (Seattle, Oct. 2002), and makes the case for developing passive or active immunoprophylaxis in neonates to prevent mother-to-infant transmission. Macaque studies have shown that passive transfer of NAb combinations (for example, IgG1b12, 2G12, 2F5, and 4E10; or 2G12 and 2F5) can confer partial or complete protection to infant macaques from subsequent oral SHIV challenge. Safrit *et al.* [2004] (**immunoprophylaxis**, **mother-to-infant transmission**)
- 2F5: A complex of the epitope peptide ELDKWAS bound to 2F5 was crystalized, and the peptide was found to interact with amino acids near the base of the very long (22 residue) CDR 3H region of the Ab. Ala substitution of the CDR H3 region confirmed the importance of these sites near the base of the H3 loop for interaction with the epitope in the context of intact gp41 as well as the peptide. A Phe at the apex of the loop was not located directly in the binding site, however binding of 2F5 to the epitope was very sensitive to non-conservative substitutions in this position (F100G, F100H, and F100R); these diminished both binding affinity and 2F5 neutralization, suggesting a role for the very long CDR 3H region. The authors suggest that particularly long CDR H3 regions may be a common feature of HIV-1 NAbs, based on the 22 residues in H3 of 2F5, the 18 H3 residues in b12, and the 22 H3 residues in X5. They express concern that because small animals like mice are unable to elicit Ab responses with such long H3s, they may be poor model systems for HIV vaccine studies. Zwick *et al.* [2004]
- 2F5: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. gp41 NAbs 2F5 and 4E10 are able to potently neutralize the SOS pseudovirion post-attachment, although 2F5 performed relatively poorly in the pre-attachment assay, a further support for previous studies that indicated it does not bind well to native Env, and may bind best after the virus is attached to cells. Binley *et al.* [2003]
- 2F5: A sCD4-17b single chain chimera was made that can bind to the CD4 binding site, then bind and block co-receptor interaction. This chimeric protein is a very potent neutralizing agent, more potent than IgG1b12, 2G12 or 2F5 against Ba-L infection of CCR5-MAGI cells. It has potential for prophylaxis or therapy. Dey *et al.* [2003]
- 2F5: Four newborn macaques were challenged with pathogenic SHIV 89.6 and given post exposure prophylaxis using a combination of NAbs 2F5, 2G12, 4E10 and IgG1b12. 2/4 treated animals did not show signs of infection, and 2/4 macaques maintained normal CD4+ T cell counts and had a lower delayed peak viremia compared to the controls. Ferrantelli *et al.* [2003]
- 2F5: This study investigates the effects of glycosylation inhibitors on the binding between HIV-1 gp120 and mannose-binding lectin (MBL). Mannosidase I inhibitor deoxymannojirimycin (dMM) inhibits formation of complex and hybrid N-linked saccharides and yields virus with more mannose residues. dMM added during viral production significantly enhanced the binding 2F5 and 2G12, but not IgG1b12 in a viral capture assay. Hart *et al.* [2003]
- 2F5: MAbs IgG1b12, 2G12, 2F5 and 4E10 were tested for their ability to neutralize two primary HIV-1 clade A isolates (UG/92/031 and UG/92/037) and two primary HIV-1 clade D isolates (UG/92/001 and UG/92/005). 4E10 demonstrated the most potent cross-neutralization activity. Quadruple administration of MAbs IgG1b12, 2G12, 2F5, and 4E10 induced strong synergistic neutralization of 4 clade A isolates (UG/92/031, UG/92/037, RW/92/020 and RW/92/025) as well as 5 clade D isolates (UG/92/001,UG/9/005, /93/086/RUG/94/108, UG/94/114). The authors note this combination of 4 MAbs neutralizes primary HIV A, B, C, and D isolates. Kitabwalla *et al.* [2003]
- 2F5: This review dicusses the importance and function of protective antibody responses in animal model studies in the context of effective vaccine development. SHIV models have shown protection using high levels of MAbs can prevent infection, and partial protection that can influence disease course can be obtained from modest levels of NAbs. SHIV challenges studies conducted with infusions of combinations of MAbs b12, 2G12, and 2F5 are reviewed. Mascola [2003]
- 2F5: Cyclic peptides ELLELDKWASLW that adopt constrained beta-turn conformation of the 2F5 epitope beta-turn in the complexed crystal structure were synthesized and optimize 2F5 binding affinity. This peptide elicits high titer peptide-specific immune responses in guinea pigs that do not neutralize; the authors propose this may be the result of a short CDR3 loop in guinea pigs. McGaughey *et al.* [2003]
- 2F5: AC10 is a subject who was given treatment early after infection, and had a viral rebound after cessation of therapy, which then declined to a low level. The polyclonal sera from AC10 could potently neutralize the rebound virus, and NAb escape followed with a neutralizing response against the escape variant and subsequent escape from that response. Viral loads remained low in this subject despite escape. The rebound isolate that was potently neutralized by autologous sera was not

particularly neutralization sensitive, as it resisted neutralization by sCD4 and MAbs IgG1b12, 2G12 and 2F5, and was only moderately sensitive to sera from other HIV+ individuals that had high titers of NAbs to TCLA strains. Montefiori *et al.* [2003]

- 2F5: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. 2F5 recognized most variants from 3/4 individuals by gp41 WB; the 4th individual had the ELDKWA variant Aldkwa in all three isolates. The other single Env that was not recognized carried eldRwa. Ohagen *et al.* [2003]
- 2F5: Most plasma samples of patients from early infection had NAb responses to early autologous viruses, and NAbs against heterologous strains tended to be delayed. Serial plasma samples were tested against serial isolates, and neutralization escape was shown to be rapid and continuous throughout infection. Autologous neutralization-susceptible and resistant viruses from four patients were tested for susceptability to neutralizing Ab responses using MAbs 2G12, IgG1b12 and 2F5. No correlation was established, all viruses tested were susceptible to at least one of the neutralizing MAbs. Two patients that did not have an autologous NAb response also did not evolve changes in susceptibility to these MAbs, while one patient with a pattern of autologous neutralization and escape acquired a 2G12 sensitive virus at month 6, and lost IgG1b12 sensitivity at month 21. Richman *et al.* [2003]
- 2F5: Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. Wang [2003]
- 2F5: The broadly neutralizing antibodies 2F5 and 2G12 were class-switched from IgG to IgA and IgM isotypes. Neutralizing potency was increased with valence for 2G12 so the IgM form was most potent, but for 2F5 the IgG form was most potent. Eight primary isolates were tested including two subtype A isolates. The polymeric IgM and IgA Abs, but not the corresponding IgGs, could interfere with HIV-1 entry across a mucosal epithelial layer, although they were limited in a standard neutralization assay. All isotypes could interact with activated human sera, presumably through complement, to inhibit HIV replication. Wolbank *et al.* [2003]
- 2F5: A combination of MAbs 2F5 and 2G12 given in multiple infusions was found to be safe and well tolerated even in high doses in a phase I study of seven HIV-1 infected healthy volunteers—the median elimination half-life was 7.94 days for 2F5, and 16.48 for 2G12—no anti-2F5 or anti-2G12 IgM or IgG responses were detected—although there was some transient increases, overall plasma viral RNA levels decreased in 6/7 volunteers, by a median of 0.62 log_10 Armbruster *et al.* [2002]
- 2F5: IgG1b12 neutralized many South African (5/8) and Malawian (4/8) clade C primary HIV-1 isolates, being more effective than 2F5 which neutralized only two Malawian and no South African isolates. 2G12 did not neutralize any of the 16 isolates. Bures *et al.* [2002]
- 2F5: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate, with the exception of F240 which bound both equally well, which captured more virus than any other human MAb tested, and didn't neutralize either isolate. F240 enhanced the binding of CD4BS MAbs IgG1b12 and F105 and the gp41 MAb 2F5 for both R5X4 and R5 isolates. F240 also enhanced neutralization of the R5X4 isolate by 2F5, but had no effect on R5 virus. Anti-V3 MAb B4a1 did not impact 2F5 neutralization. Cavacini *et al.* [2002]
- 2F5: A modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. Chakrabarti *et al.* [2002]
- 2F5: Six sera from HIV-exposed uninfected individuals(EU) had IgA neutralizing activity dominated by recognition of a distinctive epitope within gp41, QARILAV – sera of QAFILAV-immunized BALB/c mice was neutralizing with the dose-dependent behavior similar to 2F5. Clerici *et al.* [2002a]
- 2F5: Review of NAbs that notes that 2F5 alone or in combination with other MAbs can protect some macaques against SHIV infection, that it is safe and well tolerated in humans, and that illustrates gp41's conformational change and exposure of the 2F5 epitope in the transient pre-hairpin form. Ferrantelli & Ruprecht [2002]
- 2F5: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I and Cluster II MAbs required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor, binding to a fusion intermediate. 2F5 behaved very differently than these non-neutralizing antibodies: it bound to Env in the absence of target cells, and it was distributed evenly all over the cell surface, not localized in fusion domains. It did not interact with cells that exhibited cytoplasmic mixing. 2F5 was unusual in that it exhibited temperature dependence, and did not interact below 19 degrees C, in contrast to 2G12, M77 98-6 and IgG1b12 which bound strongly at temperatures ranging between 4-37 degrees. The authors suggest the temperature dependence of 2F5 may be due to encreased flexibility of the Envelope spike at warmer temperatures facilitating epitope exposure. Finnegan *et al.* [2002]
- 2F5: Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other MAb against gp41 tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. Follis *et al.* [2002]
- 2F5: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs target-

ing fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. Golding *et al.* [2002b]

- 2F5: UK1-br and MACS2-br are R5 isolates derived from brain tissue samples from AIDS patients with dementia and HIV-1 encephalitis; both are neurotropic, but only UK1-br induced neuronal apoptosis and high levels of syncytium formation in macrophages. UK1-br Env had a greater affinity for CCR5 than MACS-br, and required low levels of CCR5 and CD4 for cell-to-cell fusion and single round infection. PBMC infected with UK1-br and MACS2-br virus isolates were resistant to neutralization by MAb 2G12. UK1-br was more sensitive than MACS2-br to IgG1b12, 2F5 and CD4-IgG2 neutralization. This pattern of Ab reactivity was similar to the to CD4-independent varient ADA197N/K, and thought to result from conformational changes which better expose the CCR5 binding regions, although the loss of the particular N-linked glycosylation site in the V1V2 stem region of ADA was experimentally shown to not be responsible for the the CD4-independent phenotype of UK1-br. Gorry *et al.* [2002]
- 2F5: HIV-1 gp160ΔCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160ΔCT with a reconstituted membrane ten-fold better than the same protein on beads (except for the YU2 form that doesn't bind 2F5)—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160ΔCT PLs indistinguishably from gp160ΔCT expressed on the cell surface. Grundner *et al.* [2002]
- 2F5: ELDKWAS was embedded into a beta-turn-like conformational site on a framework of an antibody specific for human leukocyte antigen HLA-DR – this construct was recognized by 2F5, and is suggested as an adjuvant-independent vaccine candidate. Ho *et al.* [2002]
- 2F5: A mouse MAb was raised against a variant of ELDKWA core epitope of the NAb 2F5, eldEwa, derived from the 2F5 neutralization resistant variant MVP5180. 2F5 does not bind to the variants eldEwa, elNkwa (B.TH.TH936705) or elEkwa, while 14D9 binds only to eldEwa and not ELDKWA. The eldEwa variant is common in the HIV-1 O group. Huang *et al.* [2002]
- 2F5: DP178 is a peptide derived from the C-term heptad repeat of gp41 that is a potent inhibitor of viral-mediated fusion—it contains the 2F5 epitope but fails to stimulate 2F5-like NAbs upon immunization—the peptide was extended to force an increase in helicity, and the modified peptide had a increase in affinity for 2F5, but upon guinea pig immunization although high peptide-specific Ab titers were achieved the sera were incapable of viral neutralization—the authors propose that 2F5 may bind with low affinity to a maturation intermediate, which may account for its breadth and why it is hard to recreate the epitope, but also suggests that the high concentrations required for neutralization are not relevant *in vivo* Joyce *et al.* [2002]
- 2F5: A 2F5 anti-idiotype murine MAb Ab2/3H6 was developed that blocks 2F5 binding to a synthetic epitope peptide and to gp160 in an ELISA competition assay – Ab2/3H6 diminished the neutralizing potency of 2F5 – Ab2/3H6 Fab fragments were capable of inducing neutralizing Abs and 2F5-epitope specific responses in immunized B6D2F1 mice. Kunert *et al.* [2002]
- 2F5: A polyepitope vaccine was designed based on three repeats of the 2F5 core epitope ELDKWA combined with the V3 region peptide GPGRAFY. Abs raised in mice could recognize the peptides, sgp41, and CHO-WT cells that expressed HIV-1 Env on their surface. Li *et al.* [2002]
- 2F5: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies. Liu *et al.* [2002]
- 2F5: Rhesus macaques were better protected from vaginal challenge with SHIV89.6D (MAb 2G12, 2/4; MAbs 2F5/2G12, 2/5; and HIVIG/2F5/2G12, 4/5 infected) than from intravenous challenge (MAb 2G12, 0/3; MAbs 2F5/2G12, 1/3; and HIVIG/2F5/2G12, 3/6 infected)– the animals that were infected by vaginal challenge after Ab infusion had low or undetectable viral RNA levels and modest CD4 T-cell decline. Mascola [2002]
- 2F5: ELDKWAS co-crystallized bound to the Fab' 2F5 fragment showed the epitope peptide in a type I beta-turn conformation. Pai *et al.* [2002]
- 2F5: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 – SOS gp140-2F5-IgG1b12 formed multiple ring structures composed of two SOS gp140 proteins bridged by two Ab molecules, while 2F5 and 2G12 formed extended chains rather than closed rings. Schulke *et al.* [2002]
- 2F5: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – 2F5 recognized o-gp140. Srivastava *et al.* [2002]
- 2F5: The antiviral response to intravenously administered MAbs 2F5 and 2G12 was evaluated in 7 HAART-naive asymptomatic HIV-1 infected patients during a treatment period of 28 days. MAb therapy reduced plasma HIV RNA in 3/7 patients during the treatment period, and transiently reduced viral load in two more. CD4 counts were up in 3/7 through day 28, and transiently increased in three more. Vigorous complement activation was observed after 48/56 Ab infusions. Before treatment, 2F5 neutralized isolates from five patients and no escape was observed during treatment. Stiegler *et al.* [2002]
- 2F5: Expanding the minimal epitope ELDKWA to an end-capped, linear nonapeptide, Ac-LELDKWASL-amide attained maximal affinity within a set of native gp41-sequence peptides – scanning single residue substitutions confirmed that essential recognition requirements were the central DKW core sequence and the importance of the terminal Leu residues for high-affinity binding – high specificity binding pockets at central Lys and Trp side-chains and an absolute requirement for the carboxylate group of the Asp side chain were found – the nine

residue fragment flanked by pairs of Ser and constrained by a disulfide bridge had high affinity for 2F5. Tian *et al.* [2002]

- 2F5: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b]
- 2F5: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. Xu *et al.* [2002]
- 2F5: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002]
- 2F5: ELNKWA is an escape variant not recognized by the broadly neutralizing MAb 2F5, which recognizes the core epitope ELDKWA – Abs were raised against the peptide escape variant CGELNKWAGELNKWA linked to KLH carrier – these polyclonal antibodies, like the monoclonal antibody TH-Ab1 also raised to ELNKWA, could recognize ELDKWA and escape mutant peptide epitopes ELEKWA and ELDEWA. Dong *et al.* [2001]
- 2F5: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonates macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline. Hofmann-Lehmann *et al.* [2001]
- 2F5: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to antibody 2F5. Kolchinsky *et al.* [2001]
- 2F5: Review of studies in macaques that have shown immune control of pathogenic SHIV viremia, improved clinical outcome, and protection, and the implications of the observations for HIV vaccines. Mascola & Nabel [2001]
- 2F5: Moore and colleagues review the data concerning the lack of a clear relationship between genetic subtype and serotype – 2F5 is considered in some detail, as it represents a rare vulnerability from the neutralizing antibody perspective, although while it is apparently linear, attempts to present the peptide to the immune system have failed to elicit neutralizing Abs. Moore *et al.* [2001]
- 2F5: Matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS) in combination with proteolytic protection was used to identify the functional epitope for MAb 2F5, NEQELLELDKWASLWN, in the disulfide bond associated gp120/gp41 protein SOS-gp140 (JRFL) – this minimal epitope is much larger than the ELDKWA core epitope previously defined by peptide ELISA, and this could help explain why ELDKWA-peptides are poor immunogens in terms of eliciting a 2F5-like antibody response. Parker *et al.* [2001]
- 2F5: A peptide called 5-Helix was designed that binds to the C-peptide region of gp41 – 5-Helix is a potent inhibitor of HIV-1 entry that binds immediately COOH-terminal to the C-peptide region targeted by 5-Helix – the conformation of the bound 2F5 epitope is a hairpin turn. Root *et al.* [2001]
- 2F5: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. Si *et al.* [2001]
- 2F5: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12. Spenlehauer *et al.* [2001]
- 2F5: 4E10 binds proximal to 2F5 and neutralizes primary isolates of clades A, B, C, D, and E – viruses that were resistant to 2F5 were neutralized by 4E10 and vice versa. Stiegler *et al.* [2001]
- 2F5: A phage peptide library was screened with MAb 2F5, and from the peptides that bound the amino acids DKW were found to be most critical for binding – the mimetic peptide RDWSFDRWSLSEFWL elicited a cross-reactive Ab response to gp41 when used to immunize rabbits. Tumanova *et al.* [2001]
- 2F5: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001]
- 2F5: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10. Xu *et al.* [2001]
- 2F5: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b),

and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. York *et al.* [2001]

- 2F5: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three mAbs with respect to monomeric and oligomeric env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers. Zeder-Lutz *et al.* [2001]
- 2F5: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – the minimal 2F5 epitope is determined to be EQELLELDKWASLW, based on screening a gp160 fragment expression library, longer than previous studies – broadly neutralizing MAbs 2F5, IgG1b12, and 4E10 and Z13 fail to neutralize different subsets of viruses. Zwick *et al.* [2001b]
- 2F5: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2. Zwick *et al.* [2001c]
- 2F5: Paper uses IgG1 form of 2F5 – a triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the plasma half-life was 4.2 +/- 0.8 days. Baba *et al.* [2000]
- 2F5: MAbs 98-6 and 2F5 both bind to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, and to C43 alone but not to N51 alone – 98-6 and 2F5 have comparable affinities for C43, but 98-6 has a higher affinity for the complex and 2F5 may bind to an epitope of C43 that is directly involved with complex formation –and IgG1 rec form of the Ab was used in this study. Gorny & Zolla-Pazner [2000]
- 2F5: 2F5 is a candidate for immunotherapy, but generally IgG1 has a longer half life in humans than IgG3, so the isotype was switched – rec CHO-derived MAb 2F5 IgG1kappa and hybridoma-derived MAb 2F5 IgG3kappa displayed identical specificity, *in vitro* function, and epitope (ELDKWA) – it remains to be determined if isotype switching will prolongs beta-clearance. Kunert *et al.* [2000]
- 2F5: Low levels of anti-ELDKWA antibodies are observed in HIV-1 + individuals, so a C-domain P2 peptide linked to a carrier was used to immunize mice and rabbits, and stimulated a high-level anti-ELDKWA response. Liao *et al.* [2000]
- 2F5: ELDKWA peptide vaccine study. Lu *et al.* [2000c]
- 2F5: ELDKWA peptide vaccine study. Lu *et al.* [2000b]
- 2F5: Because HIV-1 is most often transmitted across mucosal surfaces, the ability of passive transfer of infused HIVIG/2F5/2G12 to protect against mucosal exposure of macaques to pathogenic SHIV 89.6PD was studied – HIVIG/2F5/2G12 protected 4/5 animals against vaginal challenge, 2F5/2G12 combined protected 2/5 animals, and 2G12 alone protected 2/4 animals – in contrast, Mascola and coworkers had previously shown single MAbs could not protect against intervenous challenge – Ab treated animals that got infected through vaginal innoculation had low viral loads and only modest declines in CD4 counts – the infused Abs were detected in the nasal, vaginal, and oral mucosa. Mascola *et al.* [2000]
- 2F5: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs. Nyambi *et al.* [2000]
- 2F5: A mini-review of observations of passive administration of IgG NAbs conferring protection against intervenous or vaginal SHIV challenge, that considers why IgG MAbs might protect against mucosal challenge. Robert-Guroff [2000]
- 2F5: 2F5 or sCD4-IgG chimeric immunoadhesin were transferred into 3T3 cells, incorporated into a collagen structure called the neo-organ, and transplanted into SCIDhu mice that were then challenged with MN or LAI – the continuous production of the therapeutic molecules in this context resulted in dramatic reduction of viral load. Sanhadji *et al.* [2000]
- 2F5: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) – 2F5 did not bind efficiently to these constructs, presumably because of the YU2 strain has a substitution in the 2F5 epitope (ALDKWA instead of ELDKWA) Yang *et al.* [2000]
- 2F5: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs. Beddows *et al.* [1999]
- 2F5: Combinations of HIVIG, 2F5, 2G12 were administered in passive-transfer experiments 24 hours prior to challenge with pathogenic SHIV 89.6PD – 3/6 animals given HIVIG/2F5/2G12 were completely protected, the others had reduced viremia and normal CD4 counts – 1/3 monkeys given 2F5/2G12 showed transient infection, the other two had reduced viral load – all monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia, although animals that got HIVIG or 2G12 had a less profound CD4 T cell decline. Mascola *et al.* [1999]
- 2F5: A meeting summary presented results regarding neutralization –MAbs 2G12 and 2F5 tested for their ability to neutralize primary isolate infection of genetically engineered cell lines (cMAGI and others, presented by T. Matthews, A. Trkola, J. Bradac) – an advantage of such cells lines over PBMCs is that markers (X-Gal) can be added for staining to simplify the assay – the consensus of the meeting was that these engineered cell lines did not improve the sensitivity of detection of primary

isolate neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization *in vitro* corresponded to efficacy *in vivo*. Montefiori & Evans [1999]

- 2F5: In a study of 116 HIV-1 + individuals, Ab reactivity to a peptide encompassing the ELDKWA peptide decreased in CDC stage C patients compared with stage A patients, and longitudinal studies showed a decline in 6/8 patients, while overall Ab reactivity to rec soluble gp160 stayed constant. Muhlbacher *et al.* [1999]
- 2F5: Review of the neutralizing Ab response to HIV-1. Parren *et al.* [1999]
- 2F5: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice b12 escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs. Poignard *et al.* [1999]
- 2F5: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection. Andrus *et al.* [1998]
- 2F5: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D. Connor *et al.* [1998]
- 2F5: The ELDKWA epitope was inserted into the antigenic site B of influenza hemagglutinin and expressed on baculovirus infected insect cells, flanked by 3 additional random amino acids, xELDKWAxx – FACS was used to isolate the clone that displayed the epitope with the most markedly increased binding capacity for 2F5, to identify particularly specific immunogenic constructs – PELDKWAPP was a high affinity form selected by FACS. Ernst *et al.* [1998]
- 2F5: Points out that 2G12 and 2F5, potent neutralizing antibodies, were identified by screening for cell surface (oligomeric Envelope) reactivity. Fouts *et al.* [1998]
- 2F5: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events. Frankel *et al.* [1998]
- 2F5: The natural immune response to the epitope of 2F5, ELDKWA, was studied in perinatally infected children and levels of reactivity to this epitope were correlated with absolute CD4 numbers over time and health status – 3/10 children who had no antibody reactivity to ELDKWA had substitutions in the epitope (ALDKWA, ELDQWA, and KLDKWA) – 2F5 competed with the ELDKWA-reactive sera depending on the serum titer. Geffin *et al.* [1998]
- 2F5: Used as a control in the study of anti-gp41 MAb NC-1 – 2F5 does not react with HIV-2 gp41 or gp160. Jiang *et al.* [1998]
- 2F5: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods – in contrast to Geffin98, where multiple pediatric sera were found to compete with 2F5, cross-competition was noted to be very rare in sera from HIV+ adults – Kunert *et al.* propose that because there is a binding site of human complement factor H which overlaps the 2F5 binding site, it may generally be masked from the immune system – 2F5 also has a remarkably long CDR3 loop of 22 amino acids, and this region could not be readily assigned to any described D(H) fragment, leading to the suggestion of recombination of two fragments from novel regions. Kunert *et al.* [1998]
- 2F5: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) Li *et al.* [1998]
- 2F5: This MAb and the results of Ugolini *et al.* [1997] are discussed – the authors propose that an Ab bound to gp41 would typically project less from the surface of the virion and so be unable to interfere with attachment Parren *et al.* [1998a]. Parren *et al.* [1998a]; Ugolini *et al.* [1997]
- 2F5: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope. Parren *et al.* [1998b]
- 2F5: Induces complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML. Takefman *et al.* [1998]
- 2F5: A wide range of neutralizing titers was observed that was independent of co-receptor usage – 2F5 was the most potent of the MAbs tested. Trkola *et al.* [1998]
- 2F5: A neutralization assay was developed based on heminested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. Yang *et al.* [1998]
- 2F5: This review summarizes results about 2F5: it binds extracellularly, near the transmembrane domain, it is the only gp41 MAb that is neutralizing, it reacts with many non-B clade viruses and has a paradoxically weak binding to virus, given the neutralizing titers. Burton & Montefiori [1997]
- 2F5: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 mug per ml for 90% viral inhibition – the isolates with no 2F5 neutralizing susceptibility had the sequences ALGQWA or ELDTWA in-

stead of EDLKWA – 7/9 primary isolates were neutralized, and ALDKWQ and ALDKWA were susceptible to neutralization. D'Souza *et al.* [1997]
- 2F5: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB Env – strong neutralizer of SHIV-vpu+ – all Ab combinations tested showed synergistic neutralization – 2F5 has synergistic response with MAbs 694/98-D (anti-V3), 2G12, b12, and F105. Li *et al.* [1997]
- 2F5: Using concentrations of Abs achievable *in vivo*, the triple combination of 2F5, 2G12 and HIVIG was found to be synergistic to have the greatest breadth and magnitude of response against 15 clade B primary isolates. Mascola *et al.* [1997]
- 2F5: A JRCSF variant that was selected for IgG1b12 resistance remained sensitive to MAbs 2G12 and 2F5, for combination therapy. Mo *et al.* [1997]
- 2F5: Review: MAbs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes. Moore & Trkola [1997]
- 2F5: Called IAM 2F5 – antibody mediated enhancement or inhibition seemed to be determined by isolate rather than antibody specificity – in this study, only 2F5 inhibited the entry of all the viruses studied, irrespective of their phenotype, and directly proportional to its affinity to monomeric HIV-1 gp160. Schutten *et al.* [1997]
- 2F5: Of three neutralizing MAbs (257-D, IgG1b12, and 2F5), 2F5 was the only one to inhibit the entry of all viruses studied, both SI and NSI, with a potency proportional to its affinity for monomeric gp126. Schutten *et al.* [1997]
- 2F5: Binding of anti-gp120 MAbs IgG1b12 or 654-30D does not mediate significant exposure of the gp41 epitopes for MAbs 2F5 and 50-69. Stamatatos *et al.* [1997]
- 2F5: Used to standardize polyclonal response to CD4 BS. Turbica *et al.* [1997]
- 2F5: The only MAb out of a large panel to show no correlation between viral binding inhibition and neutralization. Ugolini *et al.* [1997]
- 2F5: IgG1b12 was more potent with greater breadth than MAb 2F5 in an infection reduction assay including 35 primary isolates. Kessler II *et al.* [1997]
- 2F5: Only 4/20 Argentinian and 3/43 Swedish HIV+ sera reacted with LLELDKWASL – sera reacting with peptides that contained ELDKWA tended to have high neutralization titers – the region carboxyl terminal to EDLKWA was found to be more important for polyclonal sera AB binding, 670-675 WNWFDI – 2F5 bound most strongly to the peptide QELLELDKWA. Calarota *et al.* [1996]
- 2F5: 2F5 was infused into two chimpanzees which were then given an intravenous challenge with a primary HIV-1 isolate – both became infected, but with delayed detection and prolonged decrease in viral load relative to controls, indicating that preexisting, neutralizing antibodies (passively administered or actively elicited) affect the course of acute-phase virus replication and can be influential after the Ab can no longer be detected in the peripheral circulation. Conley *et al.* [1996]
- 2F5: Neutralizes HXB2, primary isolates, and chimeric virus with gp120 from primary isolates in an HXB2 background. McKeating *et al.* [1996]
- 2F5: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. Pincus *et al.* [1996]
- 2F5: Review: one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates. Poignard *et al.* [1996b]
- 2F5: Primary isolates from clade A, B, and E are neutralized by 2F5 – neutralization requires the LDKW motif – neutralization resistant isolates or 2F5 selected variants all had substitutions in the D or K. Purtscher *et al.* [1996]
- 2F5: Review: only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5. Sattentau [1996]
- 2F5: ELDKWAS is in a gp41 binding region for the negative regulator of complement factor H (CFH) – Abs to HIV generally do not cause efficient complement-mediated lysis, but binding of 2F5 can interfere with CHF binding, facilitating HIV destruction by complement. Stoiber *et al.* [1996]
- 2F5: Found to neutralize MN, JRCSF, and two B subtype primary isolates, but not a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs. D'Souza *et al.* [1995]
- 2F5: Broad cross-clade neutralization of primary isolates – additive neutralization in combination with anti-CD4BS MAb IgG1b12 (Called BM12) Kessler *et al.* [1995]
- 2F5: Review: binds to the only generally accepted strong neutralizing epitope outside of gp120, one of only 3 MAbs with strong broad activity against primary viruses, the others are 2G12 and IgG1b12 – unique member of epitope cluster Moore & Ho [1995] and John Moore, per comm 1996. Moore & Ho [1995]
- 2F5: MAb binding decreases the accessibility or alters the conformation of the gp41 fusion domain and of gp120 domains, including the binding site for the CD4 cell receptor. Neurath *et al.* [1995]
- 2F5: Called IAM 41-2F5 – exposed in the presence of gp120 on the cell surface, while most of gp41 is masked – binds proximal to transmembrane region. Sattentau *et al.* [1995]
- 2F5: Cross-clade primary virus neutralizing activity – LDKW defined as the core epitope. Trkola *et al.* [1995]
- 2F5: MAb generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994]
- 2F5: Called IAM-41-2F5 – neutralized lab and primary isolates – t 1/2 dissociation 122 min for the peptide, and 156 min for gp41 – core D(K/R)W – Ab resistant isolate had the sequence KLDNWA. Conley *et al.* [1994b]
- 2F5: Included in a multi-lab study for antibody characterization binding and neutralization assay comparison. D'Souza *et al.* [1994]
- 2F5: Failed to show synergy with anti-CD4 binding site IIIB neutralizing antibodies. Laal *et al.* [1994]
- 2F5: 2F5 epitope ELDKWA inserted into an immunogenic loop in influenza virus hemagglutinin can elicit IIIB, MN and RF neutralizing sera in immunized mice. Muster *et al.* [1994]

- 2F5: Broadly reactive neutralizing activity, ELDKWA is relatively conserved – neutralized 2 primary isolates. Purtscher *et al.* [1994]
- 2F5: gp41 mutation (582 A/T) that reduces neutralization of anti-CD4 binding site MAbs does not alter 2F5's ability to neutralize. Thali *et al.* [1994]
- 2F5: Synergy with combinations of CD4-based molecules in inhibition of HIV-1 Env mediated cell fusion. Allaway *et al.* [1993]
- 2F5: Called IAM-41-2F5 – reports MAb to be IgG1 – the gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 2F5 is not affected. Klasse *et al.* [1993a]
- 2F5: DKWA defined as the core sequence – highly conserved epitope neutralizing MAb. Buchacher *et al.* [1992]; Muster *et al.* [1993]

No. 718
MAb ID polyclonal
HXB2 Location gp160 (659–670)
Author Location gp41 (659–670)
Epitope ELLELDKWASLW
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade *HIV component:* gp41 *Adjuvant:* QS21
Species (Isotype) guinea pig
References McGaughey *et al.* 2003
Keywords antibody binding site definition and exposure, binding affinity, vaccine antigen design

- 2F5: Cyclic peptides ELLELDKWASLW that adopt constrained beta-turn conformation of the 2F5 epitope beta-turn in the complexed crystal structure were synthesized and optimize 2F5 binding affinity. This peptide elicits high titer peptide-specific immune responses in guinea pigs that do not neutralize; the authors propose this may be the result of a short CDR3 loop in guinea pigs and additional recessed contact points between 2F5 and gp41. McGaughey *et al.* [2003] (**antibody binding site definition and exposure**, **vaccine antigen design**, **binding affinity**)

No. 719
MAb ID polyclonal
HXB2 Location gp160 (662–667)
Author Location gp41 (662–667)
Epitope ELDKWA
Neutralizing no
Immunogen Vaccine
HIV component: gp41
Species (Isotype) guinea pig
References Joyce *et al.* 2002

- 2F5: DP178 is a peptide derived from the C-term heptad repeat of gp41 that is a potent inhibitor of viral-mediated fusion – it contains ELDKWA but fails to stimulate 2F5-like NAbs upon immunization – the peptide was extended to force an increase in helicity, and the modified peptide had a increase in affinity for 2F5, but upon guinea pig immunization although high peptide-specific Ab titers were achieved the sera were incapable of viral neutralization – the authors propose that 2F5 may be a low affinity maturation intermediate, which may account for its breadth and why it is hard to recreate the NAb response, but also suggests that the high concentrations required for neutralization are not relevant *in vivo*. Joyce *et al.* [2002]

No. 720
MAb ID 5B2
HXB2 Location gp160 (662–667)
Author Location Env (669–674 IIIB)
Epitope ELDKWA
Neutralizing
Immunogen Vaccine
Vector/Type: peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* B clade IIIB *HIV component:* gp41
Species (Isotype) mouse (IgG)
Ab Type C-domain
References Tian *et al.* 2001

- 5B2: There is an RT specific Ab Szilvay *et al.* [1992] and a gp41 specific Ab Tian *et al.* [2001] both called 5B2. Tian *et al.* [2001]
- 5B2: Peptides GPGRAFY and ELDKWA were conjugated to keyhole limpet hemocyanin and used to raise mouse MAbs – MAb hybridomas were generated with defined specificity – 5B2 and 9G11 bind to the peptide and to rgp41. Tian *et al.* [2001]

No. 721
MAb ID 9G11
HXB2 Location gp160 (662–667)
Author Location Env (669–674 IIIB)
Epitope ELDKWA
Neutralizing
Immunogen Vaccine
Vector/Type: peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* B clade IIIB *HIV component:* gp41
Species (Isotype) mouse (IgG)
Ab Type C-domain
References Tian *et al.* 2001

- 9G11: Peptides GPGRAFY and ELDKWA were conjugated to KLH and used to raise mouse monoclonal Ab—MAb hybridomas were generated with defined specificity—5B2 and 9G11 bind to the peptide and to rgp41. Tian *et al.* [2001]

No. 722
MAb ID TH-Ab1
HXB2 Location gp160 (662–667)
Author Location gp41 (669–674)
Epitope ELNKWA
Neutralizing L P
Immunogen Vaccine
Vector/Type: peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* B clade TH936705 *HIV component:* gp41 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) rabbit (IgG1)
Ab Type C-domain
References Dong *et al.* 2001; Xiao *et al.* 2000a

• TH-Ab1: ELNKWA is an escape variant not recognized by the broadly neutralizing MAb 2F5, which recognizes the core epitope ELDKWA—Abs were raised against the peptide escape variant CGELNKWAGELNKWA linked to KLH carrier—these polyclonal antibodies, like the MAb TH-Ab1 also raised to ELNKWA, could recognize ELDKWA and escape mutant peptide epitopes ELEKWA and ELDEWA. Dong *et al.* [2001]

No. 723
MAb ID polyclonal
HXB2 Location gp160 (662–667)
Author Location gp41
Epitope ELDKWA
Neutralizing L P
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) rabbit
Ab Type C-domain
References Liao *et al.* 2000

• Low levels of anti-ELDKWA antibodies are observed in HIV-1 + individuals, so a C-domain P2 peptide linked to a carrier was used to immunize mice and rabbits, and stimulated a high-level anti-ELDKWA response in mice and rabbits – vaccine was C-TSLIHSLIEESQNQQEKNEQELLELDKWA linked to carrier peptide K/G [(KGGG)_7-K] Liao *et al.* [2000]

No. 724
MAb ID polyclonal
HXB2 Location gp160 (662–667)
Author Location gp41 (669–674)
Epitope ELDKWA
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* Env *Adjuvant:* BSA
Species (Isotype) rabbit, mouse
Ab Type C-domain
References Xiao *et al.* 2000b

• Strong epitope-specific neutralizing antibody responses were induced using a Env peptide bound to BSA, C(ELDKWAG)_4-BSA, but not full gp160. Xiao *et al.* [2000b]

No. 725
MAb ID polyclonal
HXB2 Location gp160 (662–667)
Author Location gp41 (662–667 BH10)
Epitope ELDKWA
Neutralizing L
Immunogen Vaccine
Vector/Type: influenza *Strain:* B clade BH10 *HIV component:* gp41
Species (Isotype) mouse (IgA, IgG)
Ab Type C-domain
References Muster *et al.* 1995; Muster *et al.* 1994

• Sustained ELDKWA specific IgA response in mucosa of immunized mice. Muster *et al.* [1995]

No. 726
MAb ID polyclonal
HXB2 Location gp160 (662–667)
Author Location gp120 (669–674)
Epitope ELDKWA
Neutralizing
Immunogen Vaccine
Vector/Type: protein, polyepitope *HIV component:* gp160 *Adjuvant:* BSA
Species (Isotype) rabbit
Ab Type C-domain
References Lu *et al.* 2000b; Lu *et al.* 2000c

• High titer response to ELDKWA and RILAVERYLKD was observed upon vaccination with multiple-epitope vaccine CG-GPGRAFY-G-ELDKWA-G-RILAVERYLKD conjugated to BSA, with a weak response to GPGRAFY – immunization with CG-(ELDKWA-GPGRAFY)_2-K was also tried, yielding a strong Ab response to both ELDKWA and GPGRAFY – gp160 vaccination yielded strong Ab response but not to any of the peptides studied here. Lu *et al.* [2000c,b]

No. 727
MAb ID 14D9
HXB2 Location gp160 (662–667)
Author Location gp41 (669–674 MVP5180)
Epitope ELDEWA
Subtype B, CRF01_AE, O
Neutralizing
Immunogen Vaccine
Vector/Type: peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* natural variants *HIV component:* gp41 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG1)
Ab Type adjacent to cluster II, C-term
References Huang *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, variant cross-recognition or cross-neutralization

• 14D9: This mouse MAb was raised against a variant of ELDKWA core epitope of the NAb 2F5, eldEwa, derived from the 2F5 neutralization resistance variant MVP5180. The eldEwa peptide was conjugated to the carrier protein keyhole limpet hemocyanin (KLH) and adminstered to BALB/c mice and 14D9 was prepared using standard hybridoma methods. 2F5 does not bind to the variants eldEwa, elNkwa (B.TH.TH936705) or elEkwa, while 14D9 binds only to eldEwa and not ELDKWA. The eldEwa variant is common in the HIV-1 O group. Huang *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 728
MAb ID 4E10
HXB2 Location gp160 (671–676)
Author Location gp160 (671–676 MN)
Epitope NWFDIT
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG3κ)
Ab Type C-term

Research Contact Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria, or Polymum Scientific Inc.,

References Safrit *et al.* 2004; Pugach *et al.* 2004; Opalka *et al.* 2004; Gorny & Zolla-Pazner 2004; Kitabwalla *et al.* 2003; Wang 2003; Fiebig *et al.* 2003; Ferrantelli *et al.* 2003; Binley *et al.* 2003; Ferrantelli & Ruprecht 2002; Xu *et al.* 2002; Xu *et al.* 2001; Zwick *et al.* 2001c; Zwick *et al.* 2001b; Stiegler *et al.* 2001; D'Souza *et al.* 1994; Buchacher *et al.* 1994; Buchacher *et al.* 1992

Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, assay development, assay standardization/improvement, immunoprophylaxis, interclade comparisons, mother-to-infant transmission, reversion, viral fitness, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- 4E10: This paper reviews MAbs that bind to HIV-1 Env. 4E10 binds to a region of gp41 proximal to cluster II (aa 662-676), neighboring the binding site of the broadly neutralizing MAb 2F5 and overlapping the epitope of neutralizing Fab Z13. 4E10 is the most broadly neutralizaing MAb, neutralizing primary isolates from clades A, B, C, D and CRF01 (E), although not the most potent. Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 4E10: An antigen panel representing different regions of gp41 was generated, and sera from 23 individuals were screened. Anti-gp41 titers were very high, and sera bound to many regions of gp41, there were no immunologically silent regions. Many individuals had broad responses to diverse regions. High titer responses tended to focus on the N-heptad, C-heptad and 2F5-4E10 regions, but there was no correlation between neutralization capacity of sera and the particular peptides recognized. 4E10 responded to the three antigens that carried the minimal NWFNIT epitope, but was conformation and context sensitive. Opalka *et al.* [2004] (**assay development**, **assay standardization/improvement**)
- 4E10: A primary isolate, CC1/85, was passaged 19 times in PBMC and gradually acquired increased sensitivity to FAb b12 and sCD4 that was attributed to changes in the V1V2 loop region, in particular the loss of a potential glycosylation site. The affinity for sCD4 was unchanged in the monomer, suggesting that the structural impact of the change was manifested at the level of the trimer. The passaged virus, CCcon19, retained an R5 phenotype and its neutralization susceptibility to other Abs was essentially the same as CC1/85. The IC50 for 4E10 was greater than 50 for CCcon19, and was 44 for CC1/85, so the primary virus was weakly neutralized by 4E10. Pugach *et al.* [2004] (**reversion, viral fitness**, **variant cross-recognition or cross-neutralization**)
- 4E10: This review discusses research presented at the Ghent Workshop of prevention of breast milk transmission and immunoprophylaxis for HIV-1 in pediatrics (Seattle, Oct. 2002), and makes the case for developing passive or active immunoprophylaxis in neonates to prevent mother-to-infant transmission. Macaque studies have shown that passive transfer of NAb combinations (for example, IgG1b12, 2G12, 2F5, and 4E10) can confer partial or complete protection to infant macaques from subsequent oral SHIV challenge. Safrit *et al.* [2004] (**immunoprophylaxis**, **mother-to-infant transmission**)
- 4E10: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. gp41 NAbs 2F5 and 4E10 are able to potently neutralize the SOS pseudovirion post-attachment. Binley *et al.* [2003] (**vaccine antigen design**)
- 4E10: Four newborn macaques were challenged with pathogenic SHIV 89.6 and given post exposure prophylaxis using a combination of NAbs 2F5, 2G12, 4E10 and IgG1b12. 2/4 treated animals did not show signs of infection, and 2/4 macaques maintained normal CD4+ T cell counts and had a lower delayed peak viremia compared to the controls. Ferrantelli *et al.* [2003] (**antibody interactions**, **immunoprophylaxis**, **mother-to-infant transmission**)
- 4E10: Porcine endogenous retroviruses (PERVS) are a concern in the context of procine xenotransplantation into humans; possible strategies for protection include PERV knockout animals or vaccines. Goats immunized with the PERV transmembrane protein revealed two NAb epitope, E1 and E2. E2's epitope (FEGWFN) binds to a sequence that is perfectly preserved in all PERVS and highly conserved in all gammaretroviruses: MuLV carries FEGLFN, FeLV FEGWFN, and it shares three amino acids with the core epitope for the anti-HIV human neutralizing MAb 4E10, (LWNWFN). Fiebig *et al.* [2003]
- 4E10: MAbs IgG1b12, 2G12, 2F5 and 4E10 were tested for their ability to neutralize two primary HIV-1 clade A isolates (UG/92/031 and UG/92/037) and two primary HIV-1 clade D isolates (UG/92/001 and UG/92/005). 4E10 demonstrated the most potent cross-neutralization activity. Quadruple administration of MAbs IgG1b12, 2G12, 2F5, and 4E10 induced strong synergistic neutralization of 4 clade A isolates (UG/92/031, UG/92/037, RW/92/020 and RW/92/025) as well as 5 clade D isolates (UG/92/001,UG/9/005, /93/086/RUG/94/108, UG/94/114). The authors note this combination of 4 MAbs neutralizes primary HIV A, B, C, and D isolates. Kitabwalla *et al.* [2003] (**antibody interactions**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **mother-to-infant transmission**, **inter-clade comparisons**)
- 4E10: Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. Wang [2003] (**vaccine antigen design**, **review**)
- 4E10: Review of NAbs illustrating gp41's conformational change and exposure of the 4E10/Z13 epitope in the transient pre-hairpin form. Ferrantelli & Ruprecht [2002] (**antibody binding site definition and exposure**)
- 4E10: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ —the combination b12+2G12+2F5 conferred partial protection against

SHIV89.6—such combinations may be useful for prophylaxis at birth and against milk born transmission—the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. Xu *et al.* [2002] (**antibody interactions**, **immunoprophylaxis**, **inter-clade comparisons**)

- 4E10: 4E10 binds proximal to 2F5 and neutralizes primary isolates of clades A, B, C, D, and E – viruses that were resistant to 2F5 were neutralized by 4E10 and vice versa. Stiegler *et al.* [2001] (**antibody binding site definition and exposure**)
- 4E10: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10. Xu *et al.* [2001] (**antibody interactions**, **inter-clade comparisons**)
- 4E10: MAbs 4E10 and Z13 both bind proximally to 2F5 to a conserved linear epitope that has some conformational aspects – both bind to MN virions, bind weakly to infected cells in a manner that is not disrupted by sCD4 and neutralize some primary isolates from clades B, C, and E – maps minimal 4E10 epitope to NWFDIT, contrary to an earlier report – different strains were refractive to neutralization by broadly neutralizing Abs IgG1b12, 2F5, Z13 and 4E10. Zwick *et al.* [2001b] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 4E10: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2. Zwick *et al.* [2001c] (**antibody interactions**)
- 4E10: MAbs generated by hybridoma, electrofusion of PBL from HIV-1 + volunteers with CB-F7 heteromyeloma cells – also binds to MHC class II proteins – anti-class II Abs are only found in HIV-1 positive people – this paper maps 4E10's binding site to AEGTDRV, gp160(823-829), but the later Zwick *et al.* study in 2001 revised the epitope location. Buchacher *et al.* [1994] (**antibody binding site definition and exposure**, **antibody generation**)
- 4E10: Included in a multi-lab study for antibody characterization, binding and neutralization assay comparison. D'Souza *et al.* [1994] (**variant cross-recognition or cross-neutralization**)

No. 729
MAb ID Z13
HXB2 Location gp160 (671–676)
Author Location gp41 (671–676 MN)
Epitope NWFDIT
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type C-term
References Gorny & Zolla-Pazner 2004; Wang 2003; Ferrantelli & Ruprecht 2002; Zwick *et al.* 2001b
Keywords antibody binding site definition and exposure, antibody generation, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- Z13: This paper reviews MAbs and Fabs that bind to HIV-1 Env. Z13 binds to a region of gp41 proximal to cluster II (aa 662-676), neighboring the binding site of the broadly neutralizing MAb 2F5 and overlapping the epitope of neutralizing MAb 4E10. Z13 is broadly neutralizing, neutralizing primary isolates from clades A, B, C, D and CRF01 (E). Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **review**)
- Z13: Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. Wang [2003] (**vaccine antigen design**, **review**)
- Z13: Review of NAbs that notes Z13 is a phage display generated FAb fragment from a B clade infected individual and that illustrates gp41's conformational change and exposure of the 4E10/Z13 epitope in the transient pre-hairpin form. Ferrantelli & Ruprecht [2002] (**antibody binding site definition and exposure**, **antibody generation**)
- Z13: MAb 4E10 and FAb Z13 both bind proximally to 2F5 to a relatively conserved linear epitope that has some conformational aspects – both bind to MN virions, bind weakly to infected cells in a manner that is not disrupted by sCD4 and can neutralize some primary isolates from clades B, C, and E – Z13 was selected using a phage display library with the MN gp41 peptide LLELDKWASLWNWFDITNWSW from an HIV infected donor who had an exceptionally broad NAb response – different strains were refractive to neutralization by broadly neutralizing Abs IgG1b12, 2F5, Z13 and 4E10 – epitope location noted here is by analogy to MAb 4E10. Zwick *et al.* [2001b] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**)

No. 730
MAb ID B30
HXB2 Location gp160 (720–734)
Author Location gp41 (720–734 BH10)
Epitope HLPIPRGPDRPEGIE
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
Research Contact George Lewis
References Abacioglu *et al.* 1994

- B30: Epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 731
MAb ID polyclonal
HXB2 Location gp160 (724–745)
Author Location gp41 (731–752)
Epitope PRGPDRPEGIEEEGGERDRDRS
Neutralizing
Immunogen Vaccine

Vector/Type: Cowpea mosaic virus *Strain:* B clade IIIB *HIV component:* gp41
Species (Isotype) mouse (IgA, IgG2a)
References Durrani *et al.* 1998

- Comparison of intranasal and oral immunization of HIV-1 peptide expressed in a plant viral vector – intranasal gave the better response. Durrani *et al.* [1998]

No. 732
MAb ID 41S-2
HXB2 Location gp160 (725–745)
Author Location gp160 (732–750)
Epitope RGPDRPEGIEEEGGERDRDRS
Neutralizing yes
Immunogen Vaccine
Vector/Type: peptide keyhole limpet hemocyanin (KLH) conjugate *HIV component:* gp41
Species (Isotype) mouse (IgG2bκ)
References Hifumi *et al.* 2003; Hifumi *et al.* 2002; Hifumi *et al.* 2000b; Hifumi *et al.* 2000a
Keywords anti-idiotype, antibody sequence, variable domain

- 41S-2: A murine Ab called i41SL1-2 was raised against the complementary determining region of the 41S-2 light chain, CRDL-1 (RSSKSLLYSNGNTYLY). As with 41S-2-L, the light chain of i41SL1-2 also had catalytic activity and degraded the immunizing peptide, initially cleaving between the Arg1 and Ser2. i41SL1-2 did not cross-react with gp41 peptide, gp120 V3 loop peptide and bound weakly to 41S-2-L.i41SL1-2 shows homology to the anti-VIP Ab (VIP, vasoactive intestinal peptide) that also has peptidase character. Both light chains contain a catalytic triad composed of Asp, Ser, and His (for i41SL1-2: Asp73, Ser 76 or Ser70 and His 79). Intact i41SL1-2 was unable to degrade CDRL-1, possibly due to an immobile inactive conformation of the catalytic triad. Hifumi *et al.* [2003] (**anti-idiotype**, **antibody sequence, variable domain**)
- 41S-2: 41S-2-L refers to the light chain of 41S-2, which can enzymatically decompose the gp41 protein of HIV-1, but doesn't degrade unrealted proteins. The peptide RGPDRPEGIEEEGGERDRDRS, against which the MAb was raised, can also be cleaved, initially between Glu12-Gly13, followed by successive cleavage reactions. Hifumi *et al.* [2002]
- 41S-2: BALBc mice were immunized with gp41 peptide and a MAb specific for the peptide was generated – isolated MAb light chains displayed proteolytic activity toward the peptide epitope which may be due to a catalytic triad on light chain (Asp73, Ser76, and His79) – no catalytic activity was observed for the whole antibody. Hifumi *et al.* [2000a]
- 41S-2: The complementary determining region of 41S-2-L, the light chain of 41S-2, is strongly involved in gp41 recognition. This light chain can serve as a molecular catalyst for gp41 degredation. Hifumi *et al.* [2000b]

No. 733
MAb ID 447-52D (447/52-DII, 447-52-D, 447d, 447-52-D, 447-D, 447, 447D)
HXB2 Location gp160 (726–729)
Author Location gp120 (MN)
Epitope GPXR
Subtype B
Neutralizing L P
Immunogen HIV-1 infection
Species (Isotype) human (IgG3λ)
Ab Type V3
Research Contact Dr. Susan Zolla-Pazner, NYU Med Center NY, NY; Veteran Affairs Med Center NY, NY; or Cellular Products Inc, Buffalo, NY,
References Sharpe *et al.* 2004; Pugach *et al.* 2004; Pinter *et al.* 2004; McCaffrey *et al.* 2004; Ling *et al.* 2004; Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Kessler *et al.* 2003; Binley *et al.* 2003; Poignard *et al.* 2003; Ferrantelli & Ruprecht 2002; He *et al.* 2002; Gorny *et al.* 2002; Sharon *et al.* 2002; Srivastava *et al.* 2002; Verrier *et al.* 2001; York *et al.* 2001; Park *et al.* 2000; Nyambi *et al.* 2000; Ly & Stamatatos 2000; Hioe *et al.* 2000; Grovit-Ferbas *et al.* 2000; Gorny *et al.* 2000; Beddows *et al.* 1999; Hioe *et al.* 1999; Nyambi *et al.* 1998; Gorny *et al.* 1998; Connor *et al.* 1998; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a; Parren *et al.* 1998a; Smith *et al.* 1998; Mondor *et al.* 1998; Inouye *et al.* 1998; Ugolini *et al.* 1997; Gorny *et al.* 1997; Hill *et al.* 1997; Parren *et al.* 1997b; Boots *et al.* 1997; Hioe *et al.* 1997b; Hioe *et al.* 1997a; Fouts *et al.* 1997; Binley *et al.* 1997a; D'Souza *et al.* 1997; Sattentau 1996; Trkola *et al.* 1996a; Jagodzinski *et al.* 1996; Forthal *et al.* 1995; Moore & Ho 1995; Moore *et al.* 1995a; Zolla-Pazner & Sharpe 1995; Zolla-Pazner *et al.* 1995; Sattentau *et al.* 1995; Saarloos *et al.* 1995; Fontenot *et al.* 1995; Sattentau 1995; Moore *et al.* 1994a; Gorny *et al.* 1994; VanCott *et al.* 1994; Laal *et al.* 1994; Conley *et al.* 1994a; Spear *et al.* 1993; Cavacini *et al.* 1993a; Keller *et al.* 1993; Gorny *et al.* 1993; Karwowska *et al.* 1992b; Buchbinder *et al.* 1992; Gorny *et al.* 1992
Keywords acute infection, ADCC, antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, assay development, assay standardization/improvement, binding affinity, coreceptor, complement, enhancing activity, inter-clade comparisons, kinetics, mimotopes, reversion, viral fitness, review, structure, vaccine antigen design, variant cross-recognition or cross-neutralization

- 447-52D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the

tip of the V3 loop that also can neutralize many primary isolates. Although 447-52D was selected using a peptide, it has conformational characteristics. Inter-clade cross-neutralization by anti-V3 conformation-dependent MAbs is reduced. Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **review**)

- 447-52D: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides, but was an exception in that it is cross-neutralizing. 447-52D neutralized 12/13 clade B viruses. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 447-52D: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of the V3 MAbs 694-98D and 447-52D, that both bind near the tip of the loop, was decreased by both thrombin and trypsin. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 447-52D: Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The loss of the any of three glycans within or adjacent to the V3 loop (GM299 V3), C2 (GM292 C2), C3 (GM329 C3) increased neutralization susceptibility to 447-52D, but C4 (GM438 C4) or V5 (GM454 V5) removal did not make SF162 more sensitive. V3 glycans tended to shield V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans shielded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 447-52D: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. 5/6 anti-V3 MAbs, including 447-52D, had similar binding affinity to soluble SF162 and JR-FL rgp120s, although the V3 loop differs at three positions (HigpgrafyTtgE for JR-FL and TigpgrafyAtgD for SF162). Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 447-52D: A primary isolate, CC1/85, was passaged 19 times in PBMC and gradually acquired increased sensitivity to FAb b12 and sCD4 that was attributed to changes in the the V1V2 loop region, in particular the loss of a potential glycosylation site. The affinity for sCD4 was unchanged in the monomer, suggesting that the structural impact of the change was manifested at the level of the trimer. The passaged virus, CCcon19, retained an R5 phenotype and its neutralization susceptibility to other Abs was essentially the same as CC1/85. 447-52D did not neutralize the primary or passaged variant. Pugach *et al.* [2004] (**reversion, viral fitness**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Analysis of the conformation of 447-52D in complex with the V3MN18 peptide (gp12 aa 310-329, KRKRIHIGPGRAFYTTKN) was undertaken using solid state NMR. The bound peptide had a well defined constrained structure that was in good agreement with solution NMR and crystallographic studies. Sharpe *et al.* [2004] (**structure**)
- 447-52D: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. 447-52D was able to neutralize the SOS protein better than the wildtype, but did not neutralize SOS well when added post-attachment, as the V3 loop is involved in co-receptor engagement. Binley *et al.* [2003] (**vaccine antigen design**)
- 447-52D: The Fv fragment (composed of just the light and heavy variable regions, and the smallest intact binding unit of an Ab) of 447-52 D was expressed and purified. Preliminary NMR with the peptide epitope indicates that an NMR structure determination is feasible. Kessler *et al.* [2003] (**antibody sequence, variable domain**, **structure**)
- 447-52D: This paper attempts to engineer a gp120 molecule that would focus the immune response onto the IgG1b12 epitope. Adding a glycosylation sequon (P313N) to the V3 loop knocked out binding to anti-V3 MAbs loop 2, 19b and 447-52-D. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- 447-52D: Virion capture assays are not a good predictor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – Ab 447-52D was able to potently neutralize 89.6 and to neutralize JR-CSF at a high concentration but poorly neutralized ADA – b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, but anti-V3 Abs 447-52D and 19b, which did not neutralize JR-CSF and ADA, captured amounts of p24 equal to or higher than the amounts captured by the neutralizing Ab b12. Poignard *et al.* [2003] (**antibody binding site definition and exposure**, **assay development**, **variant cross-recognition or cross-neutralization**)
- 447-52D: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain un-

affected by these loops. This was one of the V3 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- 447-52D: Review of NAbs. Ferrantelli & Ruprecht [2002]
- 447-52D: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 447-52D bound to primary isolates from all clades except CRF01 (E), was conformationally sensitive and showed the some of the most potent neutralizing activity. Gorny *et al.* [2002] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. He *et al.* [2002]
- 447-52D: The feasibility of determining the NMR structure of the V3(MN) peptide bound to the 447-52D Fab fragment was tested and a general strategy for obtaining NMR structures of V3 peptide-Fab fragments developed – preliminary NMR spectra for 447-52D complexed to a 23 amino acid V3 peptide was obtained. Sharon *et al.* [2002] (**structure**)
- 447-52D: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent—antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs—447-D recognized the gp120 monomer much more readily than o-gp140, suggesting the V3 loop is less exposed on o-gp140 and on intact virions. Srivastava *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 447-52D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – the dissociation constant, Kd of 447-52D for the cell associated primary and TCLA Envs was equal, 3nM. York *et al.* [2001] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **binding affinity**)
- 447-52D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7-10 fold preference for the oligomer. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)
- 447-52D: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. Grovit-Ferbas *et al.* [2000] (**vaccine antigen design**)
- 447-52D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – V3 MAbs 447-52-D and 268-10-D did not effect proliferation. Hioe *et al.* [2000]
- 447-52D: Called 447D – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. Ly & Stamatatos [2000] (**antibody binding site definition and exposure**)
- 447-52D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 447-52D showed the highest cross-reactivity, bound to 24/26 viruses tested, but achieved 90% neutralization only against MN, 50% against CA5, and no neutralization was observed for 3 other isolates tested. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 447-52D: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000] (**antibody binding site definition and exposure**)
- 447-52D: rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the re-

sulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – TCLA strains showed enhanced 447-52D neutralization sensitivity relative to PBMC-adapted lines (32X increase between HIV-1 (M2424/PBMC(p0)) and HIV-1 (M2424/H9(p9)) and a >128X increase between HIV-1 (W61D/PBMC) and HIV-1 (W61D/SupT1) isolates) Beddows *et al.* [1999] (**variant cross-recognition or cross-neutralization**)

- 447-52D: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs. Hioe *et al.* [1999]
- 447-52D: Review of clade specificity and anti-V3 HIV-1-Abs. Zolla-Pazner *et al.* [1999a] (**review**, **inter-clade comparisons**)
- 447-52D: MAb peptide-reactivity pattern clustered with the immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group – 447 reacted with peptides containing GPGR, but also with many lacking this sequence (GPGQ, for example), and it failed to react with 2/14 peptides containing GPGR, illustrating the importance of context. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D. Connor *et al.* [1998]
- 447-52D: Kinetic parameters were measured, and the association rates were similar, but dissociation rate constants were quite variable for V3 MAbs, 1324E was comparable to 447-52D. Gorny *et al.* [1998] (**kinetics**)
- 447-52D: Called 447-D – 447-D resistance took longer to acquire in virus with the M184V substituted RT, and had the form (AAC N to TAC Y) at position 5 of the V3 loop, rather than the GPGR to GPGR resistance found with wildtype RT. Inouye *et al.* [1998]
- 447-52D: Inhibits binding of Hx10 to both CD4 positive and negative HeLa cells. Mondor *et al.* [1998] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 447-52D was the most potent and cross-reactive of 18 human MAbs tested and was the only MAb which bound to virions from isolates CA20 (subtype F), CA13 (subtype H), and VI526 (subtype G) Nyambi *et al.* [1998] (**inter-clade comparisons**)
- 447-52D: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**antibody binding site definition and exposure**)
- 447-52D: Called 447-52-D – The tip of the MN V3 loop was inserted into cold causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and 447-52D was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN. Smith *et al.* [1998] (**vaccine antigen design**)
- 447-52D: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – 447-52D has an epitope involving the tip of the V3 loop, that was previously studied with this method Keller *et al.* [1993] – in Keller *et al.*, with no competition, LxGPxR was the most common six-mer, 38% of the peptides – after competition with a gp120 IIIB ligand (QRGPGR)i, RGPxR was the most common and one peptide had the sequence QRGPGR, showing type specific mimotopes can be enriched by strain specific ligand competition protocols Boots *et al.* [1997]. Boots *et al.* [1997]; Keller *et al.* [1993] (**antibody binding site definition and exposure**, **mimotopes**)
- 447-52D: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – many of these isolates had the GPGR motif at the apex of the V3 loop. D'Souza *et al.* [1997] (**variant cross-recognition or cross-neutralization**, **assay standardization/improvement**)
- 447-52D: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 447-52D bound monomer, oligomer, and neutralized JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- 447-52D: Used as a control for comparison to five V3 RF selected antibodies – 447-52D was reactive with A, B, and C clade peptides, but not E. Gorny *et al.* [1997] (**inter-clade comparisons**)
- 447-52D: Called 447 – gp120 can inhibit MIP-1alpha from binding to CCR5, but this inhibitory effect is blocked by preincubation of gp120 with three anti-V3 MAbs: 447, 257, 1027 – MAb 670 which binds in the C5 region had no effect. Hill *et al.* [1997] (**co-receptor**)
- 447-52D: Tested using a resting cell neutralization assay. Hioe *et al.* [1997a] (**assay standardization/improvement**)
- 447-52D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Neutralizes TCLA strains but not primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Viral binding inhibition by 447-D was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997] (**antibody binding site definition and exposure**)

- 447-52D: Called 447-52-D – The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS inhibits 447-52D binding. Jagodzinski *et al.* [1996] (**antibody binding site definition and exposure**)
- 447-52D: Review: called 447-52-D – only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5. Sattentau [1996] (**variant cross-recognition or cross-neutralization**, **review**)
- 447-52D: Neutralizes JR-FL – strongly inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a] (**co-receptor**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Called 447 – The tip of the V3 loop was presented in a mucin backbone – higher valency correlates with stronger affinity constant. Fontenot *et al.* [1995] (**vaccine antigen design**)
- 447-52D: Neutralizing (- complement), no ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995] (**ADCC**, **complement**, **enhancing activity**)
- 447-52D: Binding affected by identity of amino acids flanking GPGR core – poor breadth of primary virus neutralization. Moore *et al.* [1995a] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Review: the V3 loop motif GPGR is not common outside subtype B isolates, MAb 19b is more cross-reactive than 447-52D. Moore & Ho [1995] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Ab-mediated activation of complement on HIV+ cells is higher than Ab independent activation—what has been termed "Ab independent" in fact results in part from IgM in normal human serum that is HIV-cross-reactive. Saarloos *et al.* [1995] (**complement**)
- 447-52D: Called 447d – Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity. Sattentau *et al.* [1995] (**vaccine antigen design**)
- 447-52D: Serotyping study using flow-cytometry – bound only to GPGR V3 loop tips. Zolla-Pazner *et al.* [1995] (**antibody binding site definition and exposure**)
- 447-52D: Neutralization of primary and prototype laboratory HIV-1 isolates using a resting cell assay enhances sensitivity. Zolla-Pazner & Sharpe [1995] (**assay development**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Requires GPxR at the tip of the V3 loop, common in B clade – neutralized primary isolates. Conley *et al.* [1994a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Mild oxidation of carbohydrate moieties does not alter binding. Gorny *et al.* [1994] (**antibody binding site definition and exposure**)
- 447-52D: Neutralization synergy in combination with CD4 binding domain MAbs. Laal *et al.* [1994] (**antibody interactions**)
- 447-52D: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies. Moore *et al.* [1994a] (**acute infection**)
- 447-52D: GPGQ in MAL resulted in enhanced dissociation – GPGQ in CM234 or K14T did not bind – binding affected by identity of amino acids flanking GPGR core. VanCott *et al.* [1994] (**antibody binding site definition and exposure**)
- 447-52D: Additive neutralization of MN and SF2 when combined with CD4 binding site MAb F105 – supra-additive neutralization of RF. Cavacini *et al.* [1993a] (**antibody interactions**)
- 447-52D: Neutralizes MN and IIIB: GPGR, and binds SF2: GPGR. Gorny *et al.* [1993] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Peptide phage library showed that any of the residues ADGLMNQRS in the X position tolerated in peptides that react well with the antibody. Keller *et al.* [1993] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Complement mediated virolysis of IIIB, but not in the presence of sCD4. Spear *et al.* [1993] (**complement**)
- 447-52D: 60-fold increase in neutralization potency when combined 1:1 with human MAb 588-D. Buchbinder *et al.* [1992] (**antibody interactions**)
- 447-52D: Requires GPXR at the tip of the V3 loop – neutralizes a broad array of B clade lab isolates. Gorny *et al.* [1992] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Reacts with MN, NY5, CDC4, SF2, RF, WM52, and HXB2. Karwowska *et al.* [1992b] (**variant cross-recognition or cross-neutralization**)

No. 734
MAb ID C8
HXB2 Location gp160 (727–732)
Author Location gp41 (727–732 BH10)
Epitope PDRPEG
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
References McLain *et al.* 2001; Abacioglu *et al.* 1994; Pincus *et al.* 1993; Pincus & McClure 1993

- C8: The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged. McLain *et al.* [2001]
- C8: Epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]
- C8: Immunotoxin of C8 coupled to ricin-A does not mediate cells killing, and is not affected by sCD4. Pincus & McClure [1993]
- C8: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – C8 was used as a control – the dominant response among vaccinees was to this mid-gp41 region, but not among the infected lab workers – Abs binding this region do not neutralize, bind to infected cells, nor serve as immunotoxins. Pincus *et al.* [1993]

No. 735
MAb ID B31
HXB2 Location gp160 (727–734)
Author Location gp41 (727–734 BH10)
Epitope PDRPEGIE
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
References Abacioglu *et al.* 1994

- B31: Epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]

No. 736
MAb ID B33
HXB2 Location gp160 (727–734)
Author Location gp41 (727–734 BH10)
Epitope PDRPEGIE
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43
HIV component: gp160
Species (Isotype) mouse (IgG1)
References Bristow *et al.* 1994; Abacioglu *et al.* 1994

- B33: Epitope boundaries mapped by peptide scanning IgG1. Abacioglu *et al.* [1994]
- B33: There are two MAbs in the literature named B33, see also gp120, positions 123-142 – MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. Bristow *et al.* [1994]

No. 737
MAb ID 1576
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse
References Vella *et al.* 1993

- 1576: Not neutralizing. Vella *et al.* [1993]

No. 738
MAb ID 1578
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse
References Vella *et al.* 1993; Evans *et al.* 1989

- 1578: Core epitope: IEEE – in this study, neutralized IIIB, but not RF or MN. Vella *et al.* [1993]
- 1578: No neutralizing activity – epitope may be formed by regions from both poliovirus and HIV. Evans *et al.* [1989]

No. 739
MAb ID 1579
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse
References Vella *et al.* 1993

- 1579: Core epitope: IEEE – neutralized IIIB, but not RF or MN. Vella *et al.* [1993]

No. 740
MAb ID 1583
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse
References Sattentau *et al.* 1995; Vella *et al.* 1993; Evans *et al.* 1989

- 1583: Cytoplasmic domain, epitope not exposed at the surface of HIV-1 infected cells. Sattentau *et al.* [1995]
- 1583: Core epitope: ERDRD – Could neutralize HIV IIIB but not HIV RF. Vella *et al.* [1993]
- 1583: Neutralizing activity, less broad than 1577. Evans *et al.* [1989]

No. 741
MAb ID 1899
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse
References Vella *et al.* 1993

- 1899: Could neutralize HIV IIIB and HIV RF. Vella *et al.* [1993]

No. 742
MAb ID 1907
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse

References Vella *et al.* 1993

- 1907: Could not neutralize HIV IIIB, RF or MN. Vella *et al.* [1993]

No. 743
MAb ID 1908
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse
References Sattentau *et al.* 1995; Vella *et al.* 1993; Evans *et al.* 1989

- 1908: Cytoplasmic domain, epitope not exposed at the surface of HIV-1 infected cells. Sattentau *et al.* [1995]
- 1908: Neutralized IIIB, but not RF or MN. Vella *et al.* [1993]

No. 744
MAb ID 1909
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse
References Vella *et al.* 1993

- 1909: Neutralized HIV IIIB but not HIV RF. Vella *et al.* [1993]

No. 745
MAb ID 41-1
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse (IgMκ)
References Dalgleish *et al.* 1988; Mani *et al.* 1994

- 41-1: This antibody gp41(735-752 IIIB) Dalgleish *et al.* [1988] seems to have been named the same as a different MAb to gp41(584-609) Mani *et al.* [1994]. Dalgleish *et al.* [1988]; Mani *et al.* [1994]
- 41-1: Neutralizes HIV-1 but not HIV-2 strains. Dalgleish *et al.* [1988]

No. 746
MAb ID 41-2
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse (IgMκ)
References Dalgleish *et al.* 1988

- 41-2: Neutralizes HIV-1 but not HIV-2 strains. Dalgleish *et al.* [1988]

No. 747
MAb ID 41-3
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse (IgMκ)
References Dalgleish *et al.* 1988

- 41-3: Neutralizes HIV-1 but not HIV-2 strains. Dalgleish *et al.* [1988]

No. 748
MAb ID ED6
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen
Species (Isotype) mouse (IgM)
References Evans *et al.* 1989

No. 749
MAb ID LA9 (121-134)
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen
Species (Isotype) mouse (IgM)
References Evans *et al.* 1989

No. 750
MAb ID 1575
HXB2 Location gp160 (728–745)
Author Location gp41 (735–752 IIIB)
Epitope DRPEGIEEEGGERDRDRS
Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse
Ab Type C-term
Research Contact C. Vella, NIBSC, Potters Bar UK
References Cleveland *et al.* 2000a; Buratti *et al.* 1997; Vella *et al.* 1993; Evans *et al.* 1989

- 1575: Ab binding to IEEE suppresses neutralizing Ab binding to adjacent epitope ERDRD. Cleveland *et al.* [2000a]
- 1575: Study shows that MAb 1575 can recognize the IEEE sequence in both gp41, and in the HPG30 region of the p17 protein – motif is conserved in both regions in different HIV-1 clades. Buratti *et al.* [1997]

- 1575: Core epitope: IEEE – neutralized IIIB, but not RF or MN. Vella *et al.* [1993]
- 1575: Neutralizing activity, less broad than 1577. Evans *et al.* [1989]

No. 751
MAb ID 88-158/02
HXB2 Location gp160 (732–747)
Author Location gp41 (732–752 IIIB)
Epitope GIEEEGGERDRDRSIR
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse (IgG2b)
References Niedrig *et al.* 1992a

- 88-158/02: Mild inhibition of *in vitro* activity at high MAb concentrations – profound enhancing activity at low concentrations – significant reactivity to virion – domain non-immunogenic in humans. Niedrig *et al.* [1992a]

No. 752
MAb ID 88-158/022
HXB2 Location gp160 (732–747)
Author Location gp41 (732–752 IIIB)
Epitope GIEEEGGERDRDRSIR
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse (IgG2b)
References Niedrig *et al.* 1992a

- 88-158/022: Mild inhibition of *in vitro* activity at high MAb concentrations – profound enhancing activity at low concentrations – significant reactivity to virion – domain non-immunogenic in humans. Niedrig *et al.* [1992a]

No. 753
MAb ID 88-158/079
HXB2 Location gp160 (732–747)
Author Location gp41 (732–752 IIIB)
Epitope GIEEEGGERDRDRSIR
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse (IgG1)
References Niedrig *et al.* 1992a

- 88-158/079: Mild inhibition of HIV *in vitro* at high MAb concentrations – profound enhancing activity at low concentrations – weak binding to virion – domain non-immunogenic in humans. Niedrig *et al.* [1992a]

No. 754
MAb ID polyclonal
HXB2 Location gp160 (733–736)
Author Location gp41 (735–752 IIIB)
Epitope IEEE
Neutralizing L
Immunogen Vaccine
Vector/Type: Cowpea mosaic virus *HIV component:* gp41
Species (Isotype) mouse (IgG)
Ab Type C-term
References McLain *et al.* 2001; Cleveland *et al.* 2000b

- The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged. McLain *et al.* [2001]
- When PRGPDRPEGIEEEGGERDRDRS was used as antigen an immunodominant, non-neutralizing response to IEEE was observed, but immunization GERDRDR shifts the response to ERDRD. Cleveland *et al.* [2000b]

No. 755
MAb ID polyclonal
HXB2 Location gp160 (733–736)
Author Location gp41 (735–752 NL43)
Epitope IEEE
Neutralizing L
Immunogen Vaccine
Vector/Type: Cowpea mosaic virus *HIV component:* gp41
Species (Isotype) mouse (IgG)
Ab Type C-term
References McLain *et al.* 2001

- The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged. McLain *et al.* [2001]

No. 756
MAb ID B8
HXB2 Location gp160 (733–741)
Author Location gp41 (733–741 BH10)
Epitope IEEEGGERD
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI
HIV component: gp160
Species (Isotype) mouse (IgG1)
References Abacioglu *et al.* 1994; Pincus *et al.* 1993

- B8: Epitope boundaries mapped by peptide scanning. Abacioglu *et al.* [1994]
- B8: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – B8 was used as a control – the dominant response among vaccinees was to this mid-gp41 region, but not among the infected lab workers – Abs binding this region do not neutralize, bind to infected cells, nor serve as immunotoxins. Pincus *et al.* [1993]

No. 757
MAb ID 1577
HXB2 Location gp160 (739–743)
Author Location gp41 (735–752 IIIB)
Epitope ERDRD

Neutralizing no
Immunogen Vaccine
Vector/Type: poliovirus *Strain:* B clade IIIB *HIV component:* gp41
Species (Isotype) mouse
Ab Type C-term
Research Contact C. Vella or Morag Ferguson (NIBSC, Potters Bar UK)
References Cleveland *et al.* 2000a; Vella *et al.* 1993; D'Souza *et al.* 1991; Evans *et al.* 1989

- 1577: UK Medical Research Council AIDS reagent: ARP317.
- 1577: NIH AIDS Research and Reference Reagent Program: 1172.
- 1577: Ab binding to IEEE suppresses neutralizing Ab binding to adjacent epitope ERDRD. Cleveland *et al.* [2000a]
- 1577: Core epitope: ERDRD – could neutralize HIV IIIB and HIV RF. Vella *et al.* [1993]
- 1577: Non-neutralizing in this multi-lab study. D'Souza *et al.* [1991]
- 1577: Raised against IIIB peptide chimera – neutralized African and American HIV-1 lab strains. Evans *et al.* [1989]

No. 758
MAb ID polyclonal
HXB2 Location gp160 (739–743)
Author Location gp41 (735–752 IIIB)
Epitope ERDRD
Neutralizing L
Immunogen Vaccine
Vector/Type: Cowpea mosaic virus *HIV component:* gp41
Species (Isotype) mouse (IgG)
Ab Type C-term
References McLain *et al.* 2001; Cleveland *et al.* 2000b

- The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged. McLain *et al.* [2001]
- ERDRD-specific IgG recognizes an externalized loop of the gp41 C-terminal tail with high affinity – neutralized HIV-1 B clade strains IIIB, NL-4.3, RF, MN and D clade virus CBL-4, but HXB-2D (clade B) was not recognized – when PRGPDRPEGIEEEGGERDRDRS was used as antigen an immunodominant, non-neutralizing response to IEEE was observed, but immunization GERDRDR shifts the response to ERDRD – NAb does not inhibit attachment of free virus, but does inhibit by an event that precedes fusion-entry. Cleveland *et al.* [2000b]

No. 759
MAb ID DZ
HXB2 Location gp160 (822–855)
Author Location gp41 (827–860 BRU)
Epitope VAEGTDRVIEVVQGACRAIRHIPRRIRQGLERIL
Neutralizing L
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* Env
Species (Isotype) human (IgG1λ)
References Boyer *et al.* 1991

- DZ: Weakly neutralizing IIIB – binds to peptides 827-843 and 846-860 of BRU – reacted specifically with IIIB and RF. Boyer *et al.* [1991]

No. 760
MAb ID 2F19C
HXB2 Location gp160
Author Location gp120 (HIV2ROD)
Epitope APGK
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide *Strain:* HIV-2 ROD
Species (Isotype) mouse
Ab Type C3
References Matsushita *et al.* 1995

- 2F19C: Binds in WB, but binds poorly to Env on the cell surface, APGK is the core binding region. Matsushita *et al.* [1995]

No. 761
MAb ID 1334-D (1334, 1334D)
HXB2 Location gp160
Author Location gp120 (HIV451)
Epitope TRTSV
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Gorny *et al.* 2000; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a
Keywords antibody binding site definition and exposure

- 1334-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004]
- 1334-D: Called 1334. V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using HIV451 gp120. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 1334-D: Called 1334 – binds to V3 peptides from MN, SF2, NY5, RF, and CDC4 strains as well as x-reactivity with peptides from A, C, D, F, G, and H subtypes – was suggested to be IgG1lambda here – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7-10 fold preference for the oligomer. Gorny *et al.* [2000]

- 1334-D: Called 1334D – A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1334D showed intermediate cross-reactivity. Nyambi *et al.* [2000]
- 1334-D: This MAb was selected using oligomeric gp160 from HIV451. Zolla-Pazner *et al.* [1999a]
- 1334-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b]

IV-C-16 Env Antibodies

No. 762
MAb ID 7F11
HXB2 Location Env (397–439)
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp120
Species (Isotype) mouse
References Nilsen *et al.* 1996; Lasky *et al.* 1987

- 7F11: There is another MAb with this name that binds to integrase. Nilsen *et al.* [1996]

No. 763
MAb ID D50
HXB2 Location Env (632–655)
Author Location gp41 (642–665)
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* dimeric Env
Species (Isotype) mouse
Ab Type cluster II
Research Contact Patricia Earl and Christopher Broder, NIH
References de Rosny *et al.* 2004a; de Rosny *et al.* 2004b; Srivastava *et al.* 2002; Yang *et al.* 2000; Earl *et al.* 1997; Richardson *et al.* 1996; Binley *et al.* 1996; Earl *et al.* 1994
Keywords antibody binding site definition and exposure, antibody generation

- D50: The MAb 2F5 binds to the C-heptad and is neutralizing, but the MAb D50 binds to the C-heptad and is not neutralizing. 2F5 binds preferentially to native gp41 prior to receptor activation. D50 prefers the triggered form after receptor activation. Trapped fusion-intermediates suggest 2F5 remains present shortly after gp120 triggering by CD4, but may be lost by the time the six-helix bundle is formed. D50 binds equally to the fusion-intermediate and six-helix bundle. 2F5 neutralization seems to block a later step of the fusion process. de Rosny *et al.* [2004b] (**antibody binding site definition and exposure**)
- D50: The mechanism of 2F5 neutralization was explored, and experiments suggest it is due to interference with a late step in viral entry. sCD4 binding to gp120 triggers conformational changes in gp41 allowing formation of the six helix bundle. The NAb 2F5 preferentially bound native gp41, prior to receptor triggering, while the antibody D50 that also binds to the heptad region, near 2F5, is not neutralizing, and preferentially bound the CD4 triggered gp41. The C and N peptides that can be used to block the formation of the six helix bundle and lock gp41 in the fusion intermediate state after sCD4 triggering enabled 2F5 to bind after sCD4 triggering, while D50 was able to bind to both the peptide-trapped and sCD4 induced six helix bundle equally well, suggesting the D50 epitope is linear and more exposed after sCD4 binding. de Rosny *et al.* [2004a] (**antibody binding site definition and exposure**)
- D50: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – D50 was used to capture the o-gp140 for ELISA to test the antigencity of o-gp140 using a panel of well characterized MAbs. Srivastava *et al.* [2002]
- D50: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) Yang *et al.* [2000] (**antibody binding site definition and exposure**)
- D50: Found to bind to a linear peptide, between Env amino acids 642-655 – can be blocked by the conformation dependent MAbs D16, D17, D31, D36, D37, D40, D44, D55, D59, T37, and T45 – the region is in the immunogenic cluster two region – reactive with 9/10 HIV-1 strains tested, all except HIV-1 ADA, in which the change E659D and E662A may result in the loss of binding (ELLE to DLLA) Earl *et al.* [1997] (**antibody binding site definition and exposure**)
- D50: Thought to be a discontinuous epitope recognizing residues between 649-668 – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding. Binley *et al.* [1996] (**antibody binding site definition and exposure**)
- D50: Richardson suggests this is a linear gp41 epitope. Richardson *et al.* [1996] (**antibody binding site definition and exposure**)
- D50: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994] (**antibody generation**)

No. 764
MAb ID
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: gp120 *Adjuvant:* GM-CSF
Species (Isotype) mouse (IgG1)
References Rodríguez *et al.* 1999

• The murine Ab response to a chimeric of granulocyte-macrophage colony stimulating factor GM-CSF/gp120 in vaccinia was not higher titer that the response to a gp120-vaccinia construct, but the breadth of the Ab response was greater, in particular to the C-term region of gp120 – a cellular response of greater intensity was trigged to the GM-CSF/gp120 vaccinia construct, as measured by Elispot assay. Rodríguez *et al.* [1999]

No. 765
MAb ID
HXB2 Location Env
Author Location Env (384–467)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: hepatitis B surface antigen lipoprotein particles (HsBAg) *HIV component:* V3
Species (Isotype) macaque, rabbit
References Michel *et al.* 1993
• Immunization with recombinant HIV1 V3/HBsAg hybrid particles into rabbits or macaques elicited and maintained for several months anti-V3 or HIV-1 Env proliferative, CTL and Ab responses. Michel *et al.* [1993]

No. 766
MAb ID
HXB2 Location Env
Author Location
Epitope
Neutralizing Y
Immunogen HIV-1 infection, Vaccine

Species (Isotype) human
References Burton & Parren 2000
• This review article touches on why natural immune responses do not tend to favor potent neutralizing Ab production, and discusses possible vaccine strategies to counter this problem. Burton & Parren [2000]

No. 767
MAb ID
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Pellegrin *et al.* 1996
• Detection of an autologous NAb response in 12 patients with primary infections was delayed – for patients with a viral isolate obtained at month 1, autologous NAbs to viral isolates were generally not observed before month 6, and there was no apparent relationship between the emergence of neutralizing activity and the decrease of plasma viral load. Pellegrin *et al.* [1996]

No. 768
MAb ID
HXB2 Location Env
Author Location Env
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype)
References Berger 2002
Keywords immunotherapy
• This medical hypothesis proposes that HIV shares domains with human proteins are masked from the immune response as they are seen as self. They propose blocking the shared determinants on human proteins in the thymus with antibodies, to allow anti-self responses which are normally inhibited to occur in HIV+ people. (**immunotherapy**)

No. 769
MAb ID 102-135
HXB2 Location Env
Author Location gp41 (HAM112, O group)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* O group HAM112 *HIV component:* gp160
Species (Isotype) mouse (IgG1κ)
References Scheffel *et al.* 1999
• 102-135: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – 102-135 bound to two non-contiguous peptides in combination, assumed to form some type of helical structure, and not to either individually. Scheffel *et al.* [1999]

No. 770
MAb ID 1025
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
References Berman *et al.* 1997
• 1025: Binds to 1/7 isolates from breakthrough cases from a MN gp120 vaccine trial. Berman *et al.* [1997]

No. 771
MAb ID 105-134
HXB2 Location Env
Author Location gp41 (652–681 HAM112, O group)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* O group HAM112 *HIV component:* gp160
Species (Isotype) mouse (IgG1κ)
References Scheffel *et al.* 1999
• 105-134: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity. Scheffel *et al.* [1999]

No. 772
MAb ID 10E9

HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) mouse (IgG1)
References Papsidero *et al.* 1988

- 10E9: 100/100 HIV+ human sera could inhibit 10E9 binding. Papsidero *et al.* [1988]

No. 773
MAb ID 126-50
HXB2 Location Env
Author Location gp41 (HXB2)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG2κ)
References Xu *et al.* 1991; Robinson *et al.* 1991; Tyler *et al.* 1990; Robinson *et al.* 1990b

- 126-50: No enhancing or neutralizing activity. Robinson *et al.* [1991]
- 126-50: Specific for a conformational epitope. Xu *et al.* [1991]
- 126-50: No enhancing activity for HIV-1 IIIB. Robinson *et al.* [1990b]
- 126-50: Serves as target for antibody-dependent cellular cytotoxicity ADCC. Tyler *et al.* [1990]

No. 774
MAb ID 12H2
HXB2 Location Env
Author Location gp41 (530–677 HXB2)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: Semliki-Forest Virus *HIV component:* Env
Species (Isotype) mouse (IgMκ)
References Giraud *et al.* 1999

- 12H2: Env in a Semliki-Forest Virus (SFV) vector was used to vaccinate mice intramuscularly as naked RNA, and an Ab response was induced to Env from which 12H2 was derived – and advantage of this method is that the protein is properly expressed. Giraud *et al.* [1999]

No. 775
MAb ID 13.10 (No. 13)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Research Contact Evan Hersh and Yoh-Ichi Matsumoto
References Wisnewski *et al.* 1996; Moran *et al.* 1993; Lake *et al.* 1989

- 13.10: NIH AIDS Research and Reference Reagent Program: 377.
- 13.10: 13.10 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996]
- 13.10: Heavy (V HI) and light (V lambdaII) chain sequenced – no enhancing or neutralizing activity – called No. 13. Moran *et al.* [1993]
- 13.10: First HIV-1 specific human-mouse hybridoma that produces a MAb that binds to gp120 and gp160. Lake *et al.* [1989]

No. 776
MAb ID 1B1
HXB2 Location Env
Author Location Env
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human
Research Contact Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria
References Kunert *et al.* 1998; Purtscher *et al.* 1994; Buchacher *et al.* 1994

- 1B1: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods. Kunert *et al.* [1998]
- 1B1: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994]

No. 777
MAb ID 1D10
HXB2 Location Env
Author Location gp120 (34–55)
Epitope
Neutralizing
Immunogen Vaccine

Species (Isotype)
Research Contact Phil Berman
References Callahan *et al.* 1991

- Isolation of antibody
- 1D10: Polyanionic polysaccharides were proposed to inhibit viral functions such as binding and syncytia formation through interations mediated through the local high positive charge density in the V3 loop. The binding of this N-term binding antibody is increased by dextransulfate, in contrast to anti-V3 antibodies that are inhibited. Callahan *et al.* [1991]

No. 778
MAb ID 1F7
HXB2 Location Env
Author Location Env
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human

Research Contact Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria
References Grant *et al.* 2000; Kunert *et al.* 1998; Purtscher *et al.* 1994; Buchacher *et al.* 1994

- 1F7: There is an anti-idiotype MAb named 1F7 that was raised against pooled IgG from HIV-1 + subjects that recognizes a set of antibodies against HIV Gag, Pol, and Env, and this MAb is reported to inhibit anti-HIV CTL activity—this is not the same as the 1F7 described by Buchacher *et al.* Grant *et al.* [2000]
- 1F7: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods. Kunert *et al.* [1998]
- 1F7: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994]

No. 779
MAb ID 30D
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen
Species (Isotype)
References Yang *et al.* 2002

- 30D: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140Δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002]

No. 780
MAb ID 31710B
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen
Species (Isotype) human (IgG1)
References Alsmadi & Tilley 1998

- 31710B: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains. Alsmadi & Tilley [1998]

No. 781
MAb ID 38B5/C9
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162
HIV component: gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 38B5/C9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—38B5/C9 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. He *et al.* [2002]

No. 782
MAb ID 39H10/A11
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162
HIV component: gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 39H10/A11: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—39H10/A11 bound to three R5 and three X4 B clade viruses, as well as two E clade viruses. He *et al.* [2002]

No. 783
MAb ID 3C9
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing L
Immunogen Vaccine
Strain: B clade SF2
Species (Isotype) mouse
References Kang *et al.* 1992

Keywords anti-idiotype, vaccine antigen design, variant cross-recognition or cross-neutralization

- C39: Murine antibodies were raised against human polyclonal antibodies against gp120, pooled from HIV-1 infected individuals. One anti-idiotype MAb was shown to bind to the CD4-binding site, and this MAb could raise anti-anti-idiotype antibodies when injected into cyngomolgous monkeys. The monkey MAbs neutralized laboratory strains MN, RF, and IIIB. Kang *et al.* [1992] (**anti-idiotype**, **vaccine antigen design**, **variant cross-recognition or cross-neutralization**)

No. 784
MAb ID 3D5
HXB2 Location Env
Author Location Env
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human
Research Contact Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria
References Kunert *et al.* 1998; Purtscher *et al.* 1994; Buchacher *et al.* 1994

- 3D5: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods. Kunert *et al.* [1998]
- 3D5: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. Buchacher *et al.* [1994]

No. 785
MAb ID 3H6
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen
Species (Isotype) mouse
References Pinter *et al.* 1995

- 3H6: There is another MAb with this ID that recognizes Rev.
- 3H6: Generated in response to virus grown in protein-free medium. Pinter *et al.* [1995]

No. 786
MAb ID 40D3/C11
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 40D3/C11: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—40D3/C11 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. He *et al.* [2002]

No. 787
MAb ID 49B11/A1
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 49B11/A1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—49B11/A1 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. He *et al.* [2002]

No. 788
MAb ID 52G5/B9
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 52G5/B9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162

gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—52G5/B9 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. He *et al.* [2002]

No. 789
MAb ID 55E4/H1
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 55E4/H1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—55E4/H1 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. He *et al.* [2002]

No. 790
MAb ID 56C4/C8
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 56C4/C8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—56C4/C8 bound to some R5 and X4 B clade viruses, as well as one of two E clade viruses. He *et al.* [2002]

No. 791
MAb ID 57B6/F1
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 57B6/F1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—57B6/F1 bound some R5 and X4 B clade viruses, and no E clade viruses. He *et al.* [2002]

No. 792
MAb ID 57H5/D7
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 57H5/D7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—57H5/D7 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. He *et al.* [2002]

No. 793
MAb ID 63G4/E2
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 63G4/E2: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—63G4/E2 bound to three R5 and three X4 B clade viruses, as well as two E clade viruses. He *et al.* [2002]

No. 794
MAb ID 65B12/C5
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 65B12/C5: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—65B12/C5 bound some R5 and X4 B clade viruses, and no E clade viruses. He *et al.* [2002]

No. 795
MAb ID 694/98D
HXB2 Location Env
Author Location Env (LAI)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Ling *et al.* 2004
Keywords antibody binding site definition and exposure

- 694-98D: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of the V3 MAb 694-98D to its epitope was decreased by both thrombin and trypsin. Ling *et al.* [2004] (**antibody binding site definition and exposure**)

No. 796
MAb ID 6D8
HXB2 Location Env
Author Location gp120 (21–85)
Epitope
Neutralizing
Immunogen
Species (Isotype)
Research Contact Phil Berman
References Callahan *et al.* 1991

- Isolation of antibody
- 6D8: Polyanionic polysaccharides were proposed to inhibit viral functions such as binding and syncytia formation through interations mediated through the local high positive charge density in the V3 loop. The binding of this N-term binding antibody is increased by dextransulfate, in contrast to anti-V3 antibodies that are inhibited. Callahan *et al.* [1991]

No. 797
MAb ID 6E10
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen
Species (Isotype)
Research Contact Phil Berman
References Callahan *et al.* 1991; Berman *et al.* 1991

- Isolation of antibody Berman *et al.* [1991]
- 6E10: Polyanionic polysaccharides were proposed to inhibit viral functions such as binding and syncytia formation through interations mediated through the local high positive charge density in the V3 loop. The binding of this antibody is not inhibited by dextransulfate, in contrast to anti-V3 antibodies. Callahan *et al.* [1991]

No. 798
MAb ID 7-1054
HXB2 Location Env
Author Location gp36 (HIV-2)
Epitope
Neutralizing no
Immunogen
Species (Isotype) mouse
References Scheffel *et al.* 1999

• Binds HIV-2 gp36, used as a control in a study of group O MAbs. Scheffel *et al.* [1999]

No. 799
MAb ID 85G11/D8
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* deglycosylated gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

• 85G11/D8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—three of the MAbs were conformation dependent, but did not block sCD4 binding and were part of the same competition group—these MAbs were all raised against a deglycosylated form of gp120—they could not neutralize autologous SF162 and bound some R5 and X4 B clade viruses, and no E clade viruses. He *et al.* [2002]

No. 800
MAb ID 87E4/A8
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* deglycosylated gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

• 87E4/A8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—three of the MAbs were conformation dependent, but did not block sCD4 binding and were part of the same competition group—these MAbs were all raised against a deglycosylated form of gp120—they could not neutralize autologous SF162 and bound some R5 and X4 B clade viruses, and no E clade viruses. He *et al.* [2002]

No. 801
MAb ID 97B1/E8
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* deglycosylated gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

• 97B1/E8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—three of the MAbs were conformation dependent, but did not block sCD4 binding and were part of the same competition group—these MAbs were all raised against a deglycosylated form of gp120—they could not neutralize autologous SF162 and bound some R5 and X4 B clade viruses, and no E clade viruses. He *et al.* [2002]

No. 802
MAb ID A9
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF
Species (Isotype) mouse (IgG1)
References del Real *et al.* 1999

• A9: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – A9 was a gp120 from a BALBc reconstructed nude mouse and had VH gene 7183-2. del Real *et al.* [1999]

No. 803
MAb ID ADP421 polyclonal
HXB2 Location Env
Author Location Env
Epitope
Subtype A
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) rabbit
References Jeffs *et al.* 2004
Keywords inter-clade comparisons, vaccine antigen design

- ADP421: A set of oligomeric envelope proteins were made from six primary isolates for potenial use as vaccine antigens: 92/UG/037 (clade A), HAN2/2 (clade B), 92/BR25/025 (clade C), 92/UG/021 (clade D), 93/BR/029 (clade F) and MVP5180 (clade O). This was one of a panel of MAbs used to explore folding and exposure of well characterized epitopes. The clade C isolate BR25 is apparently misfolded, as conformation-dependent antibodies did not bind to it. ADP421 is a polyclonal rabbit sera raised against CHO-derived IIIB gp120. ADP421 bound to antigens from all clades A-F, as well as group O. Polyclonal sera raised in rabbits against these antigens cross-bound the other antigens, but none of the sera had neutralizing activity. Jeffs *et al.* [2004] (**vaccine antigen design**, **inter-clade comparisons**)

No. 804
MAb ID AG10H9
HXB2 Location Env
Author Location gp41 (717–751)
Epitope
Neutralizing
Immunogen
Species (Isotype)
Research Contact BabCO
References Ohagen *et al.* 2003
Keywords brain/CSF, variant cross-recognition or cross-neutralization

- AG10H9: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. AG10H9 recognized most variants gp41 and gp160 from 3/4 individuals by WB, but not the 4th. Ohagen *et al.* [2003] (**brain/CSF**, **variant cross-recognition or cross-neutralization**)

No. 805
MAb ID AH48
HXB2 Location Env
Author Location gp120 (V3)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Zwick *et al.* 2003
Keywords antibody generation, antibody interactions

- AH-48: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. AH48 is a novel anti-V3 Fab first used in this study. Zwick *et al.* [2003] (**antibody generation**, **antibody interactions**)

No. 806
MAb ID B4
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgM)
References del Real *et al.* 1999

- B4: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B4 was an anti-gp120 from a BALBc reconstructed nude mouse and had VH gene J606. del Real *et al.* [1999]

No. 807
MAb ID B5
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF
Species (Isotype) mouse (IgG1)
References del Real *et al.* 1999

- B5: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B5 was a gp120 specific MAb from a BALBc mouse and had VH gene J558. del Real *et al.* [1999]

No. 808
MAb ID B6
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgM)
References del Real *et al.* 1999

• B6: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B6 was a gp120 from a BALBc reconstructed nude mouse and had VH gene J558. del Real *et al.* [1999]

No. 809
MAb ID BAT267
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Fung *et al.* 1987

No. 810
MAb ID BAT401
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Fung *et al.* 1987

No. 811
MAb ID BAT509
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1
Species (Isotype) mouse (IgG1)
References Fung *et al.* 1987

No. 812
MAb ID C31
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Boyer *et al.* 1991

• C31: Broadly-reactive group specific MAb – high yield cultivation of human MAb. Boyer *et al.* [1991]

No. 813
MAb ID D1
HXB2 Location Env
Author Location gp41 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
References Otteken *et al.* 1996

• D1: MAbs D1, D16, had T37 bind to oligomeric gp160 equally well – pulse label experiments of MAb binding to noncleavable gp160 revealed that these MAbs bound with a delay, epitopes forming with a half life of 30 min. Otteken *et al.* [1996]

No. 814
MAb ID D12
HXB2 Location Env
Author Location gp41 (IIIB)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Research Contact Patricia Earl and Christopher Broder, NIH
References Yang *et al.* 2000; LaBranche *et al.* 1999; Otteken *et al.* 1996; Earl *et al.* 1997; Richardson *et al.* 1996; Broder *et al.* 1994; Earl *et al.* 1994
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, vaccine antigen design

• D12: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) Yang *et al.* [2000] (**vaccine antigen design**)
• D12: D12 was used in WB of HIV-1 transmembrane proteins in a study which showed that determinants of HIV-1 CD4 independence map outside regions required for coreceptor specificity – IIIBx, a CD4-independent variant of IIIB, has a truncated gp41. LaBranche *et al.* [1999]
• D12: MAbs D10 and D12 are very easily blocked by human sera from HIV+ individuals. Earl *et al.* [1997]
• D12: MAbs D4, D10, D11, D12, and D41 all bind only to complete oligomer – pulse label experiments of MAb binding to noncleavable gp160 revealed that these MAbs bound with a delay, epitopes forming with a half life of 30 min. Otteken *et al.* [1996] (**antibody binding site definition and exposure**)
• D12: This antibody was blocked more strongly by human sera than other anti-gp41 MAbs (D20, D43, D61, and T4) in a oligomeric ELISA assay. Richardson *et al.* [1996] (**antibody interactions**)
• D12: One of 18 MAbs (e. g. D4 and D40) that bind to a conformation-dependent epitope in gp41 that bind preferentially, but not exclusively, to oligomers – neutralizes IIIB and

SF2. Broder *et al.* [1994] (**antibody binding site definition and exposure**)
- D12: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994] (**antibody generation**)

No. 815
MAb ID D16
HXB2 Location Env
Author Location gp41 (IIIB)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *HIV component:* dimeric Env
Species (Isotype) mouse (IgG)
Research Contact Patricia Earl and Christopher Broder, NIH
References Earl *et al.* 1997; Weissenhorn *et al.* 1996; Earl *et al.* 1994

- D16: One of eleven MAbs (D16, D17, D31, D36, D37, D40, D44, D55, D59, T37, and T45) that are conformation dependent and that can block the binding of the MAb D50 that binds to the linear peptide gp41(642-665) – reactive with 9/10 HIV-1 strains all except HIV-1 ADA, which has the change E659D and E662A that may result in the loss of binding (ELLE to DLLA) Earl *et al.* [1997]
- D16: Precipitates both oligomeric gp140 and soluble monomeric gp41(21-166)that lacks the fusion peptide and membrane anchor, along with MAbs D16, D38, D40, D41, and D54. Weissenhorn *et al.* [1996]
- D16: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 816
MAb ID D4
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
References del Real *et al.* 1999

- D4: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – D4 was a gp120 from a BALBc reconstructed nude mouse and had VH gene J558. del Real *et al.* [1999]

No. 817
MAb ID D43
HXB2 Location Env
Author Location gp41 (HXB2)
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* dimeric Env
Species (Isotype) mouse (IgG)
Research Contact Patricia Earl and Christopher Broder, NIH
References Earl *et al.* 1997; Richardson *et al.* 1996; Earl *et al.* 1994

- D43: Partially conformation dependent – doesn't bind to short peptides, but does bind to the region spanning 641-683 – binding can be blocked by MAbs T3, D38 and D45 – MAbs in this competition group reacted with 9/10 HIV-1 strains, not binding to JRFL. Earl *et al.* [1997]
- D43: This is a linear gp41 epitope, mapping in the region 635-678 – human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4. Richardson *et al.* [1996]
- D43: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 818
MAb ID F223
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG3λ)
References Cavacini *et al.* 1999

- F223: binds to HIV-1 gp120 and to uninfected lymphocytes binding to a 159-kd auto-antigen expressed on most B cells and a small fraction of T and NK cells – the antibody enhances HIV-1 infection in a complement-dependent manner – F223 light chains have a strong homology with VLgamma2, the heavy chain to the germline gene VH3-H.11 – N-linked carbohydrates are key for recognition of both gp120 and the autoantigen – MAb 3D6 also uses VH3 and has autoreactivity. Cavacini *et al.* [1999]

No. 819
MAb ID F285
HXB2 Location Env
Author Location Env
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
References Wisnewski *et al.* 1996; Wisnewski *et al.* 1995

- F285: F285 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996]

No. 820
MAb ID F7
HXB2 Location Env
Author Location gp120 (IIIB)

Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF
Species (Isotype) mouse (IgG1)
References del Real *et al.* 1999

- F7: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – F7 was a gp120 specific MAb from a BALBc mouse and had VH gene 7183(81X), previously found expressed only in fetal liver. del Real *et al.* [1999]

No. 821
MAb ID Fab A12
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Binley *et al.* 1996

- Fab A12: Uncharacterized epitope – variable regions sequenced. Binley *et al.* [1996]

No. 822
MAb ID Fab A2
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
References Binley *et al.* 1996

- Fab A2: Uncharacterized epitope – variable regions sequenced. Binley *et al.* [1996]

No. 823
MAb ID Fab L9
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
References Binley *et al.* 1996

- Fab L9: Uncharacterized epitope – variable regions sequenced. Binley *et al.* [1996]

No. 824
MAb ID G12
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgM)
References del Real *et al.* 1999

- G12: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – G12 was a gp120 from a BALBc reconstructed nude mouse and had VH gene 7183-6. del Real *et al.* [1999]

No. 825
MAb ID G2
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgM)
References del Real *et al.* 1999

- G2: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – G2 was a gp120 from a BALBc reconstructed nude mouse and had VH gene Q52. del Real *et al.* [1999]

No. 826
MAb ID H2
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen
Species (Isotype) human (IgMκ)
Research Contact BioInvent, Lund, Sweden, commercial
References Muller *et al.* 1991

- H2: Anti-idiotypic MAbs (10B3 and 2All) against MAb H2 were generated by immunization of BALBc mice with H2 – they also react with seropositive sera. Muller *et al.* [1991]

No. 827
MAb ID H8
HXB2 Location Env
Author Location gp120 (IIIB)

Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgM)
References del Real *et al.* 1999

- H8: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – H8 was a gp120 from a BALBc reconstructed nude mouse and had VH gene Q52. del Real *et al.* [1999]

No. 828
MAb ID HBW4
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
References Wisnewski *et al.* 1996; Wisnewski *et al.* 1995; Moran *et al.* 1993

- HBW4: HBW4 is V H2 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996]
- HBW4: Heavy (V HII) and light (V lambdaII) chain sequenced. Moran *et al.* [1993]

No. 829
MAb ID HIVIG
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Nichols *et al.* 2002

- NYBC-HIVIG derived from patients with high NAb titers and NABI-HIVIG derived from patients with high anti-p24 Ab titers were compared in neutralizing assay against a panel of six primary isolates – both could neutralize all isolates tested but the NYBC-HIVIG dose required for 50% neutralization was of 3.2 fold lower, showing source plasmas influence the effective concentration of NAb present in HIVIG. Nichols *et al.* [2002]

No. 830
MAb ID IVI-4G6
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen Vaccine
Species (Isotype) mouse (IgG2b)
Research Contact K. Miyakoshi (Feji-Rebio Co, Tokyo, Japan)
References Yin *et al.* 2001

- IVI-4G6: A bi-specific Ab (BFA) was made by combining Fab fragments of gp41-specific MAb IVI-4G6 and CD3-specific Mab UCHT1 – the BFA suppressed HIV-1 propagation culture and eliminated latently infected cells. Yin *et al.* [2001]

No. 831
MAb ID IgA6/30lambda
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing 1
Immunogen HIV-1 exposed seronegative
Species (Isotype) human
References Berry *et al.* 2003
Country Kenya
Keywords antibody generation, antibody sequence, variable domain, genital and mucosal immunity, HIV exposed persistently seronegative (HEPS)

- A panel of anti-gp120 single-chain variable fragment (scFv) Ab was isolated from cervical B lymphocytes of unexposed uninfected Kenyan prostitutes. These Abs recognize gp120 in ELISA and using flow cytometry. IgG1b12 does not inhibit binding of the new clones to HIV, so the epitopes are distinct. Sequencing of the V genes of the scFv clones show they are unique. Berry *et al.* [2003] (**antibody generation**, **genital and mucosal immunity**, **HIV exposed persistently seronegative (HEPS)**, **antibody sequence, variable domain**)

No. 832
MAb ID IgA6/5k
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing 1
Immunogen HIV-1 exposed seronegative
Species (Isotype) human
References Berry *et al.* 2003
Country Kenya
Keywords antibody generation, antibody sequence, variable domain, genital and mucosal immunity, HIV exposed persistently seronegative (HEPS)

- A panel of anti-gp120 single-chain variable fragment (scFv) Ab was isolated from cervical B lymphocytes of unexposed uninfected Kenyan prostitutes. These Abs recognize gp120 in ELISA and using flow cytometry. IgG1b12 does not inhibit binding of the new clones to HIV, so the epitopes are distinct. Sequencing of the V genes of the scFv clones show they are unique. Berry *et al.* [2003] (**antibody generation**, **genital and mucosal immunity**, **HIV exposed persistently seronegative (HEPS)**, **antibody sequence, variable domain**)

No. 833
MAb ID IgA6/L4
HXB2 Location Env

Author Location gp120
Epitope
Neutralizing 1
Immunogen HIV-1 exposed seronegative
Species (Isotype) human
References Berry *et al.* 2003
Country Kenya
Keywords antibody generation, antibody sequence, variable domain, genital and mucosal immunity, HIV exposed persistently seronegative (HEPS)

- A panel of anti-gp120 single-chain variable fragment (scFv) Ab was isolated from cervical B lymphocytes of unexposed uninfected Kenyan prostitutes. These Abs recognize gp120 in ELISA and using flow cytometry. IgG1b12 does not inhibit binding of the new clones to HIV, so the epitopes are distinct. IgA6/4L is neutralizing. Sequencing of the V genes of the scFv clones show they are unique. Berry *et al.* [2003] (**antibody generation**, **genital and mucosal immunity**, **HIV exposed persistently seronegative (HEPS)**, **antibody sequence, variable domain**)

No. 834
MAb ID K14
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen
Species (Isotype) human (IgG1)
References Schutten *et al.* 1997; Schutten *et al.* 1996; Schutten *et al.* 1995b; Schutten *et al.* 1995a; Teeuwsen *et al.* 1990

- K14: In a study of NSI and SI virus neutralization, K14 did not influence viral entry. Schutten *et al.* [1997]
- K14: Reduced affinity for both SI and NSI viruses relative to MAb MN215, failed to neutralize SI strain. Schutten *et al.* [1995b]
- K14: Did not bind to peptides spanning gp41, but it does not react with Env deletion mutant 643-692 – does not react with HIV-2– competition experiments showed this was an immunodominant conserved epitope in HIV-1 positive sera from Europe and Africa. Teeuwsen *et al.* [1990]

No. 835
MAb ID M25
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: purified HIV-1
Species (Isotype) mouse (IgGκ)
References Watkins *et al.* 1996; di Marzo Veronese *et al.* 1985

- M25: heavy and light chains cloned and sequenced – binding requires heavy and light chain in combination, in contrast to M77. Watkins *et al.* [1996]

No. 836
MAb ID MAG 6B
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 6B: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R or G or A, 262 N/T, 368 D/R or T, 370 E/R or Q, 381 E/P, 384 Y/E, 421 K/L, 475 M/S, 477 D/V. Kang *et al.* [1994]

No. 837
MAb ID MO28
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
References Ohlin *et al.* 1989

- MO28: This antibody was raised by *in vitro* stimulation with a recombinant Env penv9 – the discontinuous epitope involves hydrophobic regions 632-646, 677-681 and 687-691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera. Ohlin *et al.* [1989]

No. 838
MAb ID MO30
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
References Ohlin *et al.* 1989

- MO30: This antibody was raised by *in vitro* stimulation with a recombinant Env penv9 – the discontinuous epitope involves hydrophobic regions 632-646, 677-681 and 687-691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera. Ohlin *et al.* [1989]

No. 839
MAb ID MO43
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
References Ohlin *et al.* 1989

- MO43: This antibody was raised by *in vitro* stimulation with a recombinant Env penv9 – the discontinuous epitope of MO43 involves hydrophobic regions 632-646, 677-681 and 687-691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera. Ohlin *et al.* [1989]

No. 840
MAb ID N2-4
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Research Contact Evan Hersh and Yoh-Ichi Matsumoto
References Robinson *et al.* 1990b

- N2-4: NIH AIDS Research and Reference Reagent Program: 528.
- N2-4: No enhancing activity for HIV-1 IIIB. Robinson *et al.* [1990b]

No. 841
MAb ID N70-2.3a
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Research Contact James Robinson, Tulane University, LA
References Takeda *et al.* 1992; Robinson *et al.* 1990a

- N70-2.3a: Fc receptor mediated enhancement of HIV-1 infection – binds a conformational site in the carboxyl half of gp120, distinct from 1.5e. Takeda *et al.* [1992]
- N70-2.3a: Broad reactivity. Robinson *et al.* [1990a]

No. 842
MAb ID P43110
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
Research Contact Advanced Biosciences (Kensington, MD)
References VanCott *et al.* 1995; di Marzo Veronese *et al.* 1992

- P43110: Does not recognized denatured form of the gp120 protein. VanCott *et al.* [1995]

No. 843
MAb ID P5-3
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Research Contact Evan Hersh and Yoh-Ichi Matsumoto
References Pincus *et al.* 1991; Robinson *et al.* 1990b

- P5-3: NIH AIDS Research and Reference Reagent Program: 378.
- P5-3: Poor immunotoxin activity when coupled to RAC – isotype specified as: IgG3lambda. Pincus *et al.* [1991]
- P5-3: No enhancing activity for HIV-1 IIIB. Robinson *et al.* [1990b]

No. 844
MAb ID T15G1
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen
Species (Isotype)
References Binley *et al.* 1999

- T15G1: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999]

No. 845
MAb ID T20
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Otteken *et al.* 1996; Earl *et al.* 1994

- T20: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T20 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially blocked CD4 binding. Sugiura *et al.* [1999]
- T20: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp140 revealed that these anti-CD4BS MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes. Otteken *et al.* [1996]
- T20: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 846
MAb ID T27
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope

Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- T27: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T27 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially blocked CD4 binding. Sugiura *et al.* [1999]
- T27: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 847
MAb ID T3
HXB2 Location Env
Author Location gp41 (HXB2)
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: tetrameric Env *HIV component:* Env
Species (Isotype) mouse (IgG)
References Yang *et al.* 2000; Zwick *et al.* 2001b; Earl *et al.* 1997; Earl *et al.* 1994

- T3: T3 partially competes with MAb Z13, but not MAb 4E10, both of which bind to gp41 proximally to the 2F5 epitope and have a broad neutralizing potential. Zwick *et al.* [2001b]
- T3: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) Yang *et al.* [2000]
- T3: Partially conformation dependent – doesn't bind to short peptides, but does bind to the region spanning 641-683 – binding can be blocked by MAbs D43, D38 and D45 – MAbs in this competition group reacted with 9/10 HIV-1 strains, not binding to JRFL. Earl *et al.* [1997]
- T3: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 848
MAb ID T30
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: tetrameric Env *HIV component:* Env
Species (Isotype) mouse
Research Contact C. Broder
References Ohagen *et al.* 2003; Earl *et al.* 1997; Earl *et al.* 1994
Keywords antibody binding site definition and exposure, antibody generation, brain/CSF, escape

- T30: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. T30 recognized most variants (10/13) gp41 by WB, and all of the gp160s. Ohagen *et al.* [2003] (**brain/CSF**, **escape**)
- T30: Binds in the region 580 to 640, but does not bind to peptides spanning this region – binding depends on N-linked glycosylation of Asn 616 – no other antibody tested inhibited binding, but binding could be inhibited by sera from HIV+ individuals. Earl *et al.* [1997] (**antibody binding site definition and exposure**)
- T30: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994] (**antibody generation**)

No. 849
MAb ID T4
HXB2 Location Env
Author Location gp41 (IIIB)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
References Srivastava *et al.* 2002; Yang *et al.* 2000; Stamatatos *et al.* 2000; Binley *et al.* 1999; Earl *et al.* 1997; Otteken *et al.* 1996; Weissenhorn *et al.* 1996; Richardson *et al.* 1996; Broder *et al.* 1994; Earl *et al.* 1994
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, vaccine antigen design

- T4: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – T4 recognized o-gp140. Srivastava *et al.* [2002] (**antibody binding site definition and exposure**)
- T4: Soluble gp140 derived from SF162, a neutralization-resistant primary isolate, and SF162AV2 a neutralization-susceptible isolate with 30 amino acids deleted from the V2 loop, were generated with or without the gp120-gp41 cleavage site intact – all forms are recognized by oligomer-specific MAb T4 and show enhanced binding of CD4i MAb 17b when sCD4 is bound – the fused forms are less efficiently recognized than the cleaved forms by polyclonal neutralizing sera from HIV-infected patients – the V3 loop is more exposed on the fused form. Stamatatos *et al.* [2000] (**vaccine antigen design**)
- T4: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41

MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) Yang *et al.* [2000] (**vaccine antigen design**)

- T4: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999] (**vaccine antigen design**)
- T4: This antibody, along with 7 others (M10, D41, D54, T6, T9, T10 and T35), can block the linear murine MAb D61, and the human MAb 246-D, which both bind to the immunodominant region near the two Cys in gp41 – most of these antibodies are oligomer dependent – all of the MAbs are reactive with ten different HIV-1 strains – members of this competition group are blocked by sera from HIV-1 + individuals. Earl *et al.* [1997] (**antibody interactions**)
- T4: MAbs T4 and T6 bind only to oligomer, and pulse chase experiments indicate that the epitope is very slow to form, requiring one to two hours. Otteken *et al.* [1996] (**antibody binding site definition and exposure**)
- T4: Does not bind to soluble monomeric gp41(21-166) that lacks the fusion peptide and membrane anchor, only to the oligomer gp140, as does T6. Weissenhorn *et al.* [1996] (**antibody binding site definition and exposure**)
- T4: one of five MAbs (T4, T6, T9, T10 and T35) in a competition group that bind to a conformation-dependent epitope in gp41 and is oligomer specific – neutralizes IIIB and SF2. Broder *et al.* [1994] (**antibody binding site definition and exposure**)
- T4: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994] (**antibody generation**)

No. 850
MAb ID m18 (M18, FAb M18)
HXB2 Location Env
Author Location Env
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
Research Contact D. S. Dimitrov
References McCaffrey *et al.* 2004; Zhang *et al.* 2003
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, vaccine antigen design, variant cross-recognition or cross-neutralization

- m18: Called M18. Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The loss of the glycan within the V3 loop (GM299 V3) or adjacent to V3 in C2 (GM292 C2), left SF162 susceptible to neturalization by FAb M18, and the glycan mutants in C3 (GM329 C3), C4 (GM438 C4), or V5 (GM454 V5) became resistant to M18 neutralization. The M18 epitope is unknown. V3 glycans tended to sheild V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans sheilded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- m18: m18 was selected from a human Fab phage display library by a new method called sequential antigen panning (SAP), using a series of antigens to screen the library to pick broadly cross-reactive isolates. The epitope of m18 is independent of CD4 binding. The phage display library was constructed using the combined bone marrow of three long term non-progressors with potent NAb activity in their sera. m18 bound to gp140s from primary isolates from clades A-F with nM affinities. The ability to block cell mediated fusion by m18 was compared to Fabs X5 and b12 for a clade A, CRF01 EA, G, and 6 clade B isolates, and the inhibitory activity of m18 was slightly lower but comparable to neutralizing Fabs b12 and X5. It also showed broad cross-neutralization; 11/15 pseudotyped Envs from primary isolates from clades A-F were inhibited in an IC50 assay at concentration less than or equal to 100 ug/ml; X5 was also tested and somewhat more potent, generally requiring lower concentrations and inhibiting 13/15 primary isolates. Zhang *et al.* [2003] (**antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 851
MAb ID multiple Fabs
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Burton *et al.* 1991

- A panel of anti-gp120 Fabs was generated by antigen selection from a random combinatorial library prepared from bone marrow from an asymptomatic individual. Burton *et al.* [1991]

No. 852
MAb ID multiple MAbs
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing

Immunogen Vaccine
Vector/Type: protein *HIV component:* gp120
Species (Isotype) mouse
References Denisova *et al.* 1996

- When gp120 was used as an immunogen, in contrast to gp120 bound to an anti-V3 MAb, few MAbs were generated and all bound better to the native than to the denatured protein – MAbs generated were: G1B12, G2F7, G9G8, G12F12, G1B8, G11F11, G9E8, G1B11, G1B6, G6F2, G2E7. Denisova *et al.* [1996]

No. 853
MAb ID multiple MAbs
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: gp120-CD4 complex *HIV component:* gp120
Species (Isotype) mouse
References Denisova *et al.* 1996

- When gp120-CD4 was used as an immunogen, in contrast to gp120 bound to an anti-V3 MAb, few MAbs were generated and all bound better to the native than to the denatured protein – MAbs generated were: CG43, CG41, CG49, CG53, CG42, CG4, CG46, CG40, CG52, CG51, CG48, CG50, CG125, CG124, CG121. Denisova *et al.* [1996]

No. 854
MAb ID multiple MAbs
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein-Ab complex *HIV component:* gp120-Mab complex
Species (Isotype) mouse
References Denisova *et al.* 1996

- When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes, as well as an array of MAbs to discontinuous epitope – 10 of 36 MAbs were mapped to linear epitopes and are mentioned elsewhere in this database, the others are: GV5H1, GV4D5, GV4G10, GV1A8, GV10H5, GV8E11, GV2H4, GV6E6, GV1F7, GV1G9, GV4G5, GV6B12, GV1E8, GV2B7, GV1B11, GV6H5, GV6G2, GV6B5, GV1E10, GV5E3, GV5B9, GV5F4, GV6G4, GV1A12, GV5C11, GV6B6, GV3C10. Denisova *et al.* [1996]

No. 855
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Neutralizing L P
Immunogen HIV-1 infection
Species (Isotype) human (IgG3)
References Scharf *et al.* 2001

- IgG3: HIVIG was separated into immunoglobulin classes and IgG3 neutralization of HIV strains X4, R5 and X4R5 strains was superior to IgG1 and IgG2, and IgG3 was also a more potent inhibitor of viral fusion – the IgG3 advantage was lost when only Fabs were considered, indicating the IgG3 neutralization efficacy is enhanced due to a longer hinge region of the heavy chain in comparison to IgG1 and IgG2. Scharf *et al.* [2001]

No. 856
MAb ID polyclonal
HXB2 Location Env
Author Location gp140 (IIIB)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB *HIV component:* gp120, gp140 *Adjuvant:* MPL-SE adjuvant, QS21
Species (Isotype) rabbit (IgG)
References Earl *et al.* 2001

- Immunization of rabbits with oligomeric gp140 induced production of higher levels of cross-reactive neutralizing Abs than immunization with gp120 – immunization of Rhesus macaques with gp140 yielded strong NAb against IIIB, modest against other lab-adapted strains, and no NAb activity against primary isolates – most neutralizing activity could not be blocked by a V3 peptide – 3/4 vaccinated macaques showed no viral replication upon intravenous challenge with SHIV-HXB2. Earl *et al.* [2001]

No. 857
MAb ID polyclonal
HXB2 Location Env
Author Location gp160 (IIIB)
Epitope
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* gp160 *Adjuvant:* aluminum hydroxide
Species (Isotype) human
References Cox *et al.* 1999

- 60 asymptomatic HIV-1 infected patients were vaccinated with rec gp160 in alum, produced in a baculovirus expression vector in insect cells (VaxSyn), 64 received placebo, and all were followed in a 5 year longitudinal study – a mean of 78% of vaccinated and 82% of those receiving placebo had demonstrable ADCC at the different time intervals in the study, and the vaccine did not enhance ADCC production – patients with rapid and slow disease progression showed similar ADCC levels. Cox *et al.* [1999]

No. 858
MAb ID polyclonal
HXB2 Location Env
Author Location gp160 (89.6)
Epitope
Neutralizing yes

Immunogen Vaccine
Vector/Type: modified vaccinia Ankara (MVA) *Strain:* B clade 89.6 *HIV component:* Env, Gag-Pol *Adjuvant:* IL-2/Ig
Species (Isotype) macaque
References Barouch *et al.* 2001b

- Four rhesus macaques were vaccinated with a modified vaccinia Ankara (MVA) vaccine that elicited strong CTL responses as well as antibody responses. The animals were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, secondary NAb responses upon challenge, partial preservation of CD4+ T-cell counts, lower viral loads, and no evidence of disease or mortality by day 168 after challenge—monkeys that got a sham vaccine had high viral load, progressed to disease, and 2/4 were dead by day 168. Barouch *et al.* [2001b]

No. 859
MAb ID polyclonal
HXB2 Location Env
Author Location gp160
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human
References Ahmad *et al.* 2001

- High CD4+ T-cell count and low viral load was correlated with high ADCC anti-HIV-1 Env Ab titers in a study of 46 HIV-1 infected individuals from all disease stages. Ahmad *et al.* [2001]

No. 860
MAb ID polyclonal
HXB2 Location Env
Author Location gp160
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Beirnaert *et al.* 2001

- Neutralizing antibodies are thought to inhibit HIV entry by blocking either binding or fusion – six broadly cross-neutralizing sera that can neutralize group M and O viruses inhibit the binding to PBMCs – the nine primary isolates tested in this study represented very diverse subtypes and recombinant forms, and different co-receptor usage. Beirnaert *et al.* [2001]

No. 861
MAb ID polyclonal
HXB2 Location Env
Author Location gp160
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Beirnaert *et al.* 2000

- Sera from 66 HIV individuals from diverse geographic locations could neutralize primary isolates to different extents: broad cross-neutralizing isolates could neutralize 14 primary isolates from HIV-1 group M clades A-H and three O isolates, limited cross-neutralizing sera neutralized some isolates, and non-neutralizing sera—6/7 broadly neutralizing sera were from African women, despite only 14/66 study subjects being women—ability to neutralize three key isolates, MN lab (envB/gagB, X4 coreceptor), VI525 (envG/gagH, envA/gagA, R5X4) and CA9 (Group O, R5) was predictive of being able to neutralize an additional set of 14 primary isolates. Beirnaert *et al.* [2000]

No. 862
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (SF2)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF2 *HIV component:* gp120 *Adjuvant:* MF59, PLG
Species (Isotype) mouse, baboon
References O'Hagan *et al.* 2000

- Microparticles were used as an adjuvant for entrapped HIV-1 gp120 and induced strong serum IgG responses in mice – polylactide co-glycolide polymer (PLG) microparticles in combination with MF-59 had the highest response. O'Hagan *et al.* [2000]

No. 863
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (SF2, US4)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA, protein *Strain:* B clade SF2, B clade US4 *HIV component:* gp120 *Adjuvant:* aluminum phosphate, MF59, PLG
Species (Isotype) macaque, guinea pig, mouse
References O'Hagan *et al.* 2001

- DNA vaccines of codon-optimized Env and Gag genes driven by CMV promotors and absorbed on to PLG microparticles were more effective than naked DNA at eliciting strong Ab responses (more rapid, higher titer, more stable), comparable to gp120 in MF-59. O'Hagan *et al.* [2001]

No. 864
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) chimpanzee (IgG)
References Moore & Burton 1999; Shibata *et al.* 1999

- polyclonal: Commentary discussing this finding noting the particularly high neutralization titer and limited breadth of the chimpanzee sera used in this study. Moore & Burton [1999]
- polyclonal: Purified IgG from chimpanzee sera infected with several HIV-1 strains was used for passive administration to macaques which were subsequently challenged with the virulent SHIV bearing the HIV-1 env DH12 – *in vitro* neutralization correlated with protection *in vivo*. Shibata *et al.* [1999]

No. 865
MAb ID polyclonal
HXB2 Location Env
Author Location gp160 (MN)
Epitope
Neutralizing L P
Immunogen HIV-1 infection
Species (Isotype) human (IgA)
References Moja *et al.* 2000

- 15 samples isolated from parotid saliva were selected for study as they had anti-Env IgA – IgA neutralizing activity was detected that was not directed at either EDELKWA or the V3 loop. Moja *et al.* [2000]

No. 866
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN, B clade SF2 *HIV component:* gp120
Species (Isotype)
References McElrath *et al.* 2000

- After 3 immunizations, 210/241 (87%) HIV-1 uninfected vaccinees in a phase II trial developed NAbs – of 140 patients receiving 4 vaccinations, 53% had persistent neutralizing antibodies to homologous virus, and 34% to heterologous virus, measured at day 728 after initial immunization – immunogens were well tolerated– but IVDUs had a decreased Ab response relative to lower risk groups. McElrath *et al.* [2000]

No. 867
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF/gp120 chimera
Species (Isotype) mouse
References Rodríguez *et al.* 1999

- The murine Ab response to a chimeric of granulocyte-macrophage colony stimulating factor GM-CSF/gp120 in vaccinia was not higher titer that the response to a gp120-vaccinia construct, but the breadth of the Ab response was greater – a cellular response of greater intensity was trigged to the GM-CSF/gp120 vaccinia construct, as measured by proliferation and Elispot. Rodríguez *et al.* [1999]

No. 868
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (YU2)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: stabilized Env trimer *Strain:* B clade HXBc2, B clade YU2 *HIV component:* Env
Species (Isotype) mouse (IgG)
Research Contact Joseph Sodroski, Harvard Medical School
References Yang *et al.* 2001

- Soluble Env trimers were created that were designed to mimic functional Env oligomers – stabilized timers could induce neutralizing antibodies more effectively than gp120, and Abs to the YU2 trimer were cross-reactive within clade B and could neutralize several primary and TCLA reactive strains – the stabilized primers did not neutralize primary isolates outside the B clade, from clades C, D, and E – HXBc2 stabilized trimer antigen elicited strong neutralizing Abs against the homologous isolate HXBc2 TCLA strain, but not against primary isolates. Yang *et al.* [2001]

No. 869
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (MN)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* aluminum hydroxide, QS21
Species (Isotype) human
References Evans *et al.* 2001

- Vaccination with QS21 adjuvant and rsgp120 elicited stronger and more sustained neutralizing antibody responses and lymphocyte proliferation with lower doses of rsgp120 than alum formulations, suggesting QS21 may be a means to reduce the does of soluble protein. Evans *et al.* [2001]

No. 870
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing yes
Immunogen HIV-1 infection
Species (Isotype) human
References Binley *et al.* 2000

- HAART inhibited the development of anti-gp120 Ab when initiated during primary infection and sometimes in patients treated within 2 years of HIV-1 infection – HAART during primary infection usually did not inhibit the development of weak NAb responses against autologous virus – 3/4 patients

intermittently adherent developed high titers of autologous NAbs, largely coincident with brief viremic periods. Binley *et al.* [2000]

No. 871
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (SIV)
Epitope
Neutralizing yes
Immunogen HIV-1 infection
Species (Isotype) macaque
References Reitter *et al.* 1998

- This study concerned an SIV mutated strain that lacked 4th, 5th and 6th sites for N-linked glycosylation – monkeys infected with the mutant viruses had increased neutralizing activity in their sera relative to monkeys infected with the parental strain. Reitter *et al.* [1998]

No. 872
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Neutralizing yes
Immunogen HIV-1 infection
Species (Isotype) human
References Kim *et al.* 2001

- After HAART reduction of viral load to <400 for three visits over a 12 month interval, 2/11 patients were found to have increased anti-Env Ab binding titers, and neutralizing Abs titers increased against primary isolates US1, and CM237 – no NAB titer increase was seen to more readily neutralized isolate BZ167 – this suggests that in certain individuals the control of HIV-1 by HAART may augment immune control of HIV. Kim *et al.* [2001]

No. 873
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Neutralizing yes
Immunogen HIV-1 exposed seronegative
Species (Isotype) human (IgA)
References Kaul *et al.* 2001b

- Kaul *et al.* provide a concise summary of the findings concerning the presence of Mucosal IgA in highly exposed, uninfected subjects, arguing for a role in protection. Kaul *et al.* [2001b]

No. 874
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF2 *HIV component:* gp120 *Adjuvant:* MF59
Species (Isotype) human
References Nitayaphan *et al.* 2000

- A phase I/II trial was conducted in 52 seronegative Thais immunizing with rgp120 SF2 – the vaccine was safe and 39/40 developed NAb responses to the autologous SF2, while 22/40 were able to cross-neutralize the heterologous strain MN. Nitayaphan *et al.* [2000]

No. 875
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (SF2)
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF2 *HIV component:* gp120, p24 Gag *Adjuvant:* Immune stimulating complexes (ISCOM)
Species (Isotype) macaque
References Heeney *et al.* 1998a

- The immune responses induced in Rhesus monkeys using two different immunization strategies was studied – one vaccine group was completely protected from challenge infection, the other vaccinees and controls became infected – protected animals had high titers of heterologous NAbs, and HIV-1-specific T helper responses – increases in RANTES, MIP 1 alpha and MIP 1 beta produced by circulating CD8+ T cells were also associated with protection. Heeney *et al.* [1998a]

No. 876
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: peptide, protein *Strain:* B clade SF2, B clade SF33 *HIV component:* gp120 *Adjuvant:* Immune stimulating complexes (ISCOM), MF59
Species (Isotype) macaque
References Verschoor *et al.* 1999

- Attempts were made to broaden immune responses induced in Rhesus monkeys by immunization of animals previously immunized that had resisted homologous challenge, with a second immunization with ISCOM-peptides or a boost with gp120 from SF33 – animals didn't survive a second challenge heterologous challenge virus SHIV(SF33) raising concerns about early antigenic sin. Verschoor *et al.* [1999]

No. 877
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF2, CRF01 CM235 *HIV component:* gp120 *Adjuvant:* MF59
Species (Isotype) baboon

References VanCott *et al.* 1999

- Immunization with rgp120 CM235 (CRF01) induced Abs capable of neutralizing TCLA subtype E (CRF01) and subtype B isolates, while rgp120SF2 induced Abs could only neutralize subtype B TCLA isolates – neither immunogen induced Abs capable of neutralizing primary HIV-1 isolates – both rgp120CM235 and rgp120SF2 induced Abs to regions within C1, V1/V2, V3, and C5, but unique responses were induced by rgp120CM235 to epitopes within C2, and by rgp120SF2 to multiple epitopes within C3, V4, and C4 – CM235 baboon sera bound 3- to 12-fold more strongly than the SF2 baboon sera to all subtype E gp120s while binding to subtype B gp120s (except SF2) were within two to threefold for the SF2 and CM235 baboon sera. VanCott *et al.* [1999]

No. 878
MAb ID polyclonal
HXB2 Location Env
Author Location gp140 (SF162DeltaV2)
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: DNA with CMV promotor *Strain:* B clade SF162 *HIV component:* gp140 *Adjuvant:* MF59
Species (Isotype) macaque, rabbit (IgG)
References Barnett *et al.* 2001

- SF162ΔV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization—when incorporated into a codon-optimized DNA vaccine with a CMV promoter and delivered by gene gun, SF162ΔV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162ΔV2, but not intact SF162, was used as the immunogen—Control MAbs 2F5 and 2G12 could neutralize all of the following primary isolates: 91US056(R5), 92US714(R5), 92US660(R5), 92HT593(R5X4), and BZ167(R5X4), while after the first protein boost, the sera from two SF162ΔV2 immunized macaques could neutralize 91US056(R5), 92US714(R5), 92US660(R5) and ADA(R5), but not 92HT593(R5X4) or 92US657(R5)—the pattern of cross-recognition shifted after the second boost. Barnett *et al.* [2001]

No. 879
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Binley *et al.* 1997b

- Retention of anti-Env antibodies and loss of anti-Gag antibodies during progression was studied, and suggested to be the result of the loss of T-cell help and the unique ability of Env to stimulate B cells even in a backdrop of declining CD4 cells, because of the ability of Env to bind to the CD4 molecule. Binley *et al.* [1997b]

No. 880
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (W61D)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade W61D *HIV component:* gp120
Species (Isotype) human
References Beddows *et al.* 1999

- rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with HIV-1 positive subjects – vaccinee sera had more potent responses to linear V1/V2 and V3 epitopes than did the sera from HIV-1 + individuals, but could only neutralize homologous or heterologous virus only after adaptation to T-cell lines – neutralization activity was lost after re-adaptation to growth in PBMCs – in contrast, sera from infected individuals could neutralize both PBMC and T-cell line adapted viruses. Beddows *et al.* [1999]

No. 881
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* Gag, gp120, V3
Species (Isotype) macaque
References Wagner *et al.* 1998b

- A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains – Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 and was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock. Wagner *et al.* [1998b]

No. 882
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA *HIV component:* gp120, gp160
Species (Isotype) mouse
References Shiver *et al.* 1997

- DNA vaccinations of BALBc mice with a gp120 or gp160 DNA vaccine elicited a strong T cell proliferative response with Th1-like secretion of gamma interferon and IL-2, with little or no IL-4, as well as antigen specific gp120 Abs. Shiver *et al.* [1997]

No. 883
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12
Species (Isotype) mouse
References Kim *et al.* 1997b

- A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice – the Ab response was detected by ELISA, but the CMN160 DNA vaccinated mice showed a neutralizing Ab response. Kim *et al.* [1997b]

No. 884
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Bradney *et al.* 1999

- Sera were taken from long term non-progressors and evidence for viral escape was noted – serum could neutralize earlier autologous isolates, but not contemporary isolates. Bradney *et al.* [1999]

No. 885
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L P
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade SF2 *HIV component:* Env, Gag
Species (Isotype) human
References Belshe *et al.* 1998

- NAbs were obtained by a HIV-1 gag/env in canary pox vaccination of eight volunteers after boosting with rgp120 against lab strains – 1/8 primary isolates was neutralized, BZ167. Belshe *et al.* [1998]

No. 886
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, Protease *Adjuvant:* MF59
Species (Isotype) human
References Belshe *et al.* 2001; Belshe *et al.* 1998

- A phase 2 trial was conducted in 435 volunteers with vCP201, a canary pox vector carrying gp120 (MN in vCP201, and SF2 in the boost), p55 (LAI) and protease (LAI), either alone or with a gp120 boost – NAbs against MN were obtained in 56% of those who received vCP201 alone, and in 94% of those who got the prime with the gp120 boost. Belshe *et al.* [1998]

No. 887
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype) human
References Neshat *et al.* 2000

- HIV-1 gp120 appears to be a B cell superantigen that binds to members of the V_{H3} Ig gene family—the gp120 binding site was localized to the Fab portion of the Ab, and discontinuous residues in the V_H region were critical. Neshat *et al.* [2000]

No. 888
MAb ID polyclonal
HXB2 Location Env
Author Location gp41 (539–684 BH10)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp41
Species (Isotype) mouse (IgG)
References Bai *et al.* 2000

- Murine rsgp41 antisera recognized a common epitope on human IFNα (aa 29-35 and aa 123-140) and on human IFNβ (aa 31-37 and aa 125-142), suggesting that elevated levels of Ab to IFNs found in HIV+ individuals may be due to a cross-reactive gp41 response. Bai *et al.* [2000]

No. 889
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (BH10)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade 89.6, B clade ADA, B clade IIIB *HIV component:* gp120 *Adjuvant:* C3d fusion
Species (Isotype) mouse (IgG)
References Ross *et al.* 2001

- gp120 was fused with murine complement protein C3d in a DNA vaccine to enhance the titers of Ab to Env – fusion to C3d resulted in a more rapid onset of Ab response and avidity maturation, after three immunizations in BALB/c mice with DNA on a gold bead delivered with a gene gun, but not in strong neutralizing Ab response. Ross *et al.* [2001]

No. 890
MAb ID polyclonal

HXB2 Location Env
Author Location gp120 (SF162DeltaV2)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: DNA prime with protein boost *Strain:* B clade SF162 *HIV component:* gp140 *Adjuvant:* MF59
Species (Isotype) macaque
References Cherpelis *et al.* 2001a; Cherpelis *et al.* 2001b

- Two animals were immunized both intradermally and intramuscularly at weeks 0, 4, and 8 with a codon optimized DNA vector expressing the SF162V2 gp140 envelope with an intact gp120-gp41 cleavage site, and both developed lymphoproliferative responses and potent neutralizing Abs – CD8+ T lymphocytes were depleted in the animals and they were challenged with SHIV162P4 – at peak viremia, plasma viral levels in the vaccinated animals were 1 to 4 logs lower than those in the unvaccinated animals. Cherpelis *et al.* [2001b]
- HIV-1 SF162ΔV2 gp140 envelope was used in a DNA-prime plus protein-boost vaccination methodology in Rhesus macaques, the animals were depleted of their CD8+ T lymphocytes, and challenged with pathogenic SHIV(SF162P4)—the vaccinated macaques had lower peak viremia, rapidly cleared virus from the periphery, and developed delayed seroconversion to SIV core antigens relative to non-vaccinated controls. Cherpelis *et al.* [2001a]

No. 891
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Sarmati *et al.* 2001

- Some HIV-1 infected patients have increasing CD4 counts despite failing ARV, and CD4 levels are correlated with HIV-1 specific NAbs – no correlation was found between NAbs and viral load in this patients. Sarmati *et al.* [2001]

No. 892
MAb ID polyclonal
HXB2 Location Env
Author Location gp41 (539–684 BH10)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp41
Species (Isotype) mouse (IgG)
References Bai *et al.* 2000

- There is a common epitope in HIV-1 gp41, and IFNalpha and IFNbeta. Bai *et al.* [2000]

No. 893
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen
Species (Isotype) human (IgM)
References Llorente *et al.* 1999

- Combinatorial antibody analysis by phage display and flow cytometry demonstrated that gp120 in HIV-1 negative people is recognized by IgM, but not IgG Abs – IgM Fab reactivity is observed throughout the entire sequence of HIV-1 IIIB gp120 and is characterized by low affinity binding and near germline configuration reflecting a lack of maturation of the IgM repertoire – no neutralizing activity was observed in a non-infected individual before isotope switching. Llorente *et al.* [1999]

No. 894
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (SF2)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF2 *HIV component:* gp120
Species (Isotype) human (IgM)
References Locher *et al.* 1999

- High risk volunteers were vaccinated with SF2 gp120 – 3 breakthrough cases were studied – SF2 neutralizing Abs were observed, but Ab titers to autologous virus were never high and took 6 months after HIV-1 infection to develop – viral loads were similar to HIV-1 infected individuals who had not been vaccinated. Locher *et al.* [1999]

No. 895
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (subtype A, B, C, D, CRF01)
Epitope
Subtype A, B, C
Neutralizing yes
Immunogen Vaccine
Vector/Type: formaldehyde-fixed whole-cell *HIV component:* gp120
Species (Isotype) mouse (IgG)
References Nunberg 2002; LaCasse *et al.* 1999

- A retraction was printed (Science 296:1025, 2002) noting that an unknown cytotoxic effect of these complex sera accounted for a major fraction of the neutralization reported in LaCasse *et al.* [1999] Nunberg [2002]. LaCasse *et al.* [1999]; Nunberg [2002]
- In this study, immunogens were generated that were thought to capture transient envelope-CD4-coreceptor structures that arise during HIV binding and fusion by formaldehyde-fixation of co-cultures of cells expressing HIV-1 Env and those expressing CD4 and CCR5 receptors – these cells elicited NAbs in CD4- and CCR5-transgenic mice that neutralized 23/24 primary isolates from clades A-E. LaCasse *et al.* [1999]

No. 896
MAb ID polyclonal
HXB2 Location Env
Author Location (B consensus)

Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Morris *et al.* 2001

- Ab responses before HAART therapy and after one year of therapy were measured in 8 individuals that were classified HAART successes, and 10 patients who were classified as HAART failures – V3 peptide antibody binding titers to the B-consensus and MN and SF2 variants, and neutralization of HIV-1 MN and four subtype B clinical isolates were tested – subjects with strong anti-V3 and NAb humoral immune responses before starting HAART were more likely to achieve sustained viral suppression to <500 copies RNA/ml on HAART – HIV-specific Ab responses declined after 1 year of successful viral suppression on HAART. Morris *et al.* [2001]

No. 897
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Pilgrim *et al.* 1997

- Sera from long-term nonprogressors(LTNP) had broader NAbs against heterologous primary isolates and were more likely to neutralize the contemporaneous autologous isolate than were sera from short-term nonprogressors and normal progressors – in 4 individuals followed from acute infection, NAbs were detected against the early autologous isolate by 5-40 weeks, and not detected in an additional 2 cases after 27-45 weeks. Pilgrim *et al.* [1997]

No. 898
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Moog *et al.* 1997

- Autologous and heterologous NAbs were studied in 18 individuals who were sampled early after sero-conversion and followed longitudinally – autologous NAbs were not detected in sera collected at the same time as the viruses were isolated – NAbs detected against the seroconversion autologous strains were not detected one year after seroconversion, and were highly specific to the virus present at the early phase of HIV infection – heterologous neutralization of primary isolates were not detected until after 2 years. Moog *et al.* [1997]

No. 899
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing yes
Immunogen HIV-1 infection
Species (Isotype) human
References Montefiori *et al.* 2001

- In 7/9 patients in whom HAART was initiated during early seroconversion, NAbs to autologous strains were not found immediately following treatment interuption after 1-3 years, and Env and Gag Abs were low or undetected by ELISA indicating, that early HAART suppresses the normal antibody response to HIV-1, presumably by limiting the concentration of viral antigens needed to drive B-cell maturation – in 3 patients with a viral rebound autologous NAbs rapidly appeared and correlated with spontaneous down-regulation of viremia – prolonged control of viremia after stopping treatment persisted in the absence of detectable NAbs, suggesting that cellular immune responses alone can control viremia under certain circumstances – these results support the notion that virus-specific B-cell priming, combined with CD8+ CTL induction, may be beneficial for HIV-1 vaccines that aim to suppress viremia in the absence of complete protection to prevent disease and reduce the rate of virus transmission. Montefiori *et al.* [2001]

No. 900
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Scala *et al.* 1999

- Random peptide libraries were screened using sera from HIV-infected subjects to identify mimotopes, peptides that mimic conformational or linear epitopes specifically recognized by Abs from HIV-1 infected individuals – the sera of simian SHIV-infected monkeys also recognized the specific peptides, and mice immunized with the selected peptides elicited HIV-specific Abs that neutralized HIV-1 isolates IIIB and NL4-3. Scala *et al.* [1999]

No. 901
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *HIV component:* mimotopes
Species (Isotype) mouse (IgG)
References Scala *et al.* 1999

- Random peptide libraries were screened using sera from HIV-infected subjects to identify mimotopes, peptides that mimic conformational or linear epitopes specifically recognized by Abs from HIV-1 infected individuals – the sera of simian SHIV-infected monkeys also recognized the specific peptides, and mice immunized with the selected peptides elicited HIV-specific Abs that neutralized HIV-1 isolates IIIB and NL4-3. Scala *et al.* [1999]

No. 902
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *HIV component:* Env, Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG)
References Lebedev *et al.* 2000

- Virus-like particles (VLPs) in the form of spherical particles with yeast dsRNA enveloped in a polysaccharide matrix carrying the protein TBI, that contains fragments of HIV Env and Gag, were used to immunize BALB/c mice and induced specific Abs against HIV-1 as measured by ELISA with TBI. Lebedev *et al.* [2000]

No. 903
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Donners *et al.* 2002

- A difference in neutralization patterns between African and European plasma is observed, especially in African women, who tended to have cross-neutralizing Abs against primary isolates. Donners *et al.* [2002]

No. 904
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Dianzani *et al.* 2002

- Immune complexes(ICs) in the plasma contained HIV RNA (80%-100%) in association with HIV-specific IgG NAbs indicating that the HIV in the plasma of carriers is frequently composed of antibody-neutralized HIV as ICs. Dianzani *et al.* [2002]

No. 905
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Kimura *et al.* 2002

- Significant neutralization activity against autologous isolates was observed in 13/19 HIV+ patients at initiation of HAART therapy which persisted during therapy, increasing in one patient, and declining in one patient – 3/6 patients with no detectable NAb at the start of therapy developed NAb responses – of the four patients with increased NAb responses, three had low level viral rebounds (blips) Kimura *et al.* [2002]

No. 906
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 exposed seronegative
Species (Isotype) human (IgA)
References Devito *et al.* 2000b

- Mucosal and plasma HIV-specific IgA that can neutralize primary isolates is present saliva (11/15 tested) and plasma (11/15) and cervicovaginal fluid (11/14) from highly exposed persistently seronegative (HEPS) individuals. Devito *et al.* [2000b]

No. 907
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 exposed seronegative
Species (Isotype) human (IgA)
References Devito *et al.* 2000a

- IgA from the genital tract, saliva and plasma from highly exposed persistently seronegative (HEPS) individuals can inhibit transcytosis of HIV-1 across a transwall system that provides a tight epithelial cell layer—50% of the IgA samples studied were able to inhibit transcytosis of at least one of two primary isolates tested, indicating this may be an important mechanism against sexual acquisition of HIV-1. Devito *et al.* [2000a]

No. 908
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype A, B, D
Neutralizing P
Immunogen HIV-1 exposed seronegative
Species (Isotype) human (IgA)
References Broliden *et al.* 2001

- IgA isolated from the saliva, genital tract, and plasma of most highly exposed persistently seronegative (HEPS) sex workers in a Kenyan cohort could neutralize a B, A and D clade primary isolates and could inhibit transcytosis of HIV across a transwall model of the human mucosal epithelium. Broliden *et al.* [2001]

No. 909
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope

Subtype A, B, D
Neutralizing P
Immunogen HIV-1 exposed seronegative
Species (Isotype) human (IgA)
References Devito *et al.* 2002

- IgA isolated from the saliva, genital tract, and plasma of most highly exposed persistently seronegative (HEPS) Kenyan sex workers mediated broad cross-clade neutralization of primary isolates (A, B, C, D, and CRF01) – 6/10 HEPS individuals that were persistently exposed to a stable HIV+ B clade infected partner showed less breadth of neutralization, and were able to neutralize clade A and B primary isolates, but not clades C, D, or CRF01. Devito *et al.* [2002]

No. 910
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 exposed seronegative
Species (Isotype) human (IgA)
References Mazzoli *et al.* 1999

- Serum HIV-specific IgA is present in highly exposed persistently seronegative individuals (HEPS) in the absence of serum IgG – serum IgA can be found in productively infected individuals and exposed seronegatives at similar titers – 5/15 sera from HEPS had neutralizing activity, 2 of these in purified IgA – HIV-1 specific serum IgA concentrations declined after one year of interruption of at-risk sex. Mazzoli *et al.* [1999]

No. 911
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 exposed seronegative
Species (Isotype) human (IgA)
References Beyrer *et al.* 1999

- HIV-specific anti-gp160 IgA is present in cervical lavage from 6/13 HIV-exposed seronegative Thai female sex workers. Beyrer *et al.* [1999]

No. 912
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade HXB2/Bal
Species (Isotype) mouse
References Chakrabarti *et al.* 2002

- A modified gp140 (gp140ΔCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. Chakrabarti *et al.* [2002]

No. 913
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype C
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6, B clade IIIB *HIV component:* Env *Adjuvant:* alpha2-macroglobin, Complete Freund's Adjuvant (CFA), GM-CSF, monophosphoryl lipid A
Species (Isotype) mouse
References Liao *et al.* 2002

- HIV-envelope peptides coupled to α2-macroglobin were much more immunogenic when formulated in monophosphoryl lipid A with GM-CSF than in complete or incomplete Freund's adjuvant or in monophosphoryl lipid A with GM-CSF alone. Liao *et al.* [2002]

No. 914
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing P
Immunogen Vaccine
Vector/Type: gp120-CD4 complex, gp140-CD4 complex *Strain:* B clade IIIB *HIV component:* gp120, gp140 *Adjuvant:* QS21
Species (Isotype) macaque
References Fouts *et al.* 2002

- gp120-CD4 and gp140-CD4 complexes were used for i.m. vaccination of rhesus macaques and neutralizing Ig was recovered using affinity chromatography using a chimeric HIV-BAL gp120 with a mimetic peptide that induces a CD4-triggered mimetic structure – the sera and affinity purified Ab were broadly neutralizing against primary X4, R5, and R5X4 isolates from multiple subtypes but did not react as well against lab-adapted isolates. Fouts *et al.* [2002]

No. 915
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Pastori *et al.* 2002

- HAART initiated during primary infection was studied in seven patients and had different effects on NAb production—in some cases, α-Env Abs were inhibited during primary infection, and in some cases strong NAbs against autologous virus were induced. Pastori *et al.* [2002]

No. 916
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) chimpanzee (IgG)
References Moore & Burton 1999; Igarashi *et al.* 1999

- The rate of virus clearance in the circulation in rhesus macaques receiving a continuous infusion of cell-free viral dual-tropic virus isolate HIV-1DH12 particles in the presence and absence of virus-specific antibodies was measured – the clearance of physical and infectious viral particles is very rapid in naive animals, with half-lives ranging from 13 to 26 minutes, but clearance cold be acheived with a half life of 3.9-7.2 minutes when chimpanzee neutralizing Abs were present to help to remove virions from the blood. Igarashi *et al.* [1999]
- polyclonal: Commentary discussing this finding noting the particularly high neutralization titer and limited breadth of the chimpanzee sera used in this study. Moore & Burton [1999]

No. 917
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* gp120, gp41 *Adjuvant:* MF59
Species (Isotype) human
References Gupta *et al.* 2002

- Different HIV strains were used for different regions: gp120 MN and gp41 LAI, rgp120 SF2.
- Vaccine trial protocol 022A in 150 HIV-1 uninfected adults (130 completed the study) showed high titer ALVAC vaccine in combination with gp120 was safe and immunogenic in HIV-1 negative volunteers – NAb responses were detected in 95% of vaccinees, with higher titers in recipients of sequential versus simultaneous dosing of the two vaccines and in vaccinia naive volunteers. Gupta *et al.* [2002]

No. 918
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade 89.6 *HIV component:* gp120, gp140 *Adjuvant:* Cholera toxin (CT), IL-12
Species (Isotype) mouse (IgA, IgG, IgG1, IgG2a)
References Albu *et al.* 2003
Keywords genital and mucosal immunity, mucosal immunity, Th1, Th2

- Mice were intranasally immunized with gp120 or gp140 with IL-12 and Cholera toxin as adjuvants. Adjuvants enhanced NAb stimulation in mucosa and genital tissues and in serum. Albu *et al.* [2003] (**genital and mucosal immunity**, **mucosal immunity**, **Th1**, **Th2**)

No. 919
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Subtype A
Neutralizing yes
Immunogen Vaccine
Vector/Type: virus-like particle (VLP) *Strain:* A clade UG5.94UG018 *HIV component:* Gag, gp120
Species (Isotype) mouse
References Buonaguro *et al.* 2002
Country Uganda
Keywords inter-clade comparisons

- BALB/c mice were immunized with VLPs carrying a subtype A gp120. Humoral immune responses directed against B-clade derived Gag (p24) peptides or gp120-Env V3 loop peptide were readily induced following a multi-dose immunization with VLP particles presenting a gp120 molecule from a HIV-1 isolate of clade A. VLP-immunized mice showed autologous and heterologous (against B-clade HIV-1 IIIB strain) neutralization activity. Proliferative responses and CTL were also observed. Buonaguro *et al.* [2002] (**inter-clade comparisons**)

No. 920
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Subtype A, B, D
Neutralizing
Immunogen Vaccine
Vector/Type: canarypox, protein *Strain:* B clade LAI, B clade MN *HIV component:* Env, Gag, Protease
Species (Isotype) human
References Cao *et al.* 2003
Country Uganda
Keywords inter-clade comparisons

- 20 Ugandan seronegative individuals were intramuscularly immunized in this study with an ALVAC HIV GagPol and Env vaccine carrying B clade agtigens.3/20 of subjects produced neutralizing antibodies against the autologous HIV-1 clade B strain MN that was T-cell line adapted; 2 also had NAb reactivity against a primary B clade cell line. No NAb cross-reaction was observed with primary viral isolates UG92029 (subtype

A) or UG92046 (subtype D). 4/20 had detectable CTL activity against B clade antigen, and one of these cross-reacted with A clade antigen, one with D clade. Cao *et al.* [2003] (**inter-clade comparisons**)

No. 921
MAb ID polyclonal
HXB2 Location Env
Author Location gp160
Epitope
Neutralizing
Immunogen SHIV infection
Species (Isotype) macaque
References Crawford *et al.* 1999
Keywords variant cross-recognition or cross-neutralization

- Neutralization assays with rsCD4, MAbs, and serum samples from SHIV-infected macaques and HIV-1 infected individuals were used to characterize the antigenic properties of the env glycoprotein of six primary isolate or TCLA SHIV variants. SHIV infected macaques could neutralize autologous virus very effectively, but serum from HXB2c or 89.6 infected animals could not neutralize heterologous SHIVs. Serum from KU infected animals could neutralize only HXB2c, and serum from 89.6PD infected animals could neutralize 89.6, 89.6P, 89.6PD and KB9 (all derived from 89.6) well. Many sera from the SHIV infected macaques could also neutralize HIV-1 strains MN and SF2. Crawford *et al.* [1999] (**variant cross-recognition or cross-neutralization**)

No. 922
MAb ID polyclonal
HXB2 Location Env
Author Location gp160
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Crawford *et al.* 1999
Keywords variant cross-recognition or cross-neutralization

- Neutralization assays with rsCD4, MAbs, and serum samples from SHIV-infected macaques and HIV-1 infected individuals were used to characterize the antigenic properties of the env glycoprotein of six primary isolate or TCLA SHIV variants. Serum from 9 HIV-1 infected people were tested for their ability to neutralize SHIVs. KU2 was least sensitive, 89.6, 89.6P, 89.6PD and KB9 (all derived from 89.6) were moderately susceptible, and SHIV HXB2c was less sensitive than IIIB, the strain from which it was derived. Crawford *et al.* [1999] (**variant cross-recognition or cross-neutralization**)

No. 923
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Subtype B, C, CRF01_AE
Neutralizing yes
Immunogen Vaccine
Vector/Type: Venezuelan equine encephalitis virus (VEE) *Strain:* B clade R2 *HIV component:* gp160ΔCT
Species (Isotype) rabbit, mouse (IgG)
References Dong *et al.* 2003
Keywords inter-clade comparisons, variant cross-recognition or cross-neutralization

- Subcutaneous or intradermal immunization with VEE replicons expressing HIV-1 R2 gp140 and with HIV-1 R2 gp160 lacking the cytoplasmic tail. Sera from 3/3 rabbits inhibited SF162 infectivity and 2/3 rabbits were able to neutralize the R2 strain.
- C3H/He mice immunized with replicons expressing RT env protein or the VEE env vector pGP expressing either gp140 or gp160 showed cross-reactive neutralizing Ab responses to five clade B env proteins, a chinese clade C strain and weakly against a chinese clade E (CRF-1) strain.
- Mice and rabbits were immunized with Venezuelan equine encephalitis virus (VEE) replicon system particles expressing HIV-1 Env from the clone R2 that was derived from a virus that was neutralization sensitive and isolated from an individual that made strong NAb resposnes. Stronger and faster NAb responses were induced with replicons expressing gp160 with the cytoplasmic tail deleted than with gp160 or gp140. NAb responses against heterologous strain SF162 were similar in BALB/c and C3H/He mice and enhanced compared to responses elicited in C57BL/6 mice. Serum from mice neutralized 5 primary clade B env proteins, a chinese clade C strain, but not a chinese clade E (CRF-1) strain. Sera from 3/3 immunized rabbits could neutralize SF162, and from 2/3 neutralized the autologous R2 strain. Dong *et al.* [2003] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 924
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype multiple, M, O
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Donners *et al.* 2003
Country Belgium
Keywords assay development, assay standardization/improvement, co-receptor, inter-clade comparisons, kinetics

- Plasma samples from six HIV-1 + Belgians showed broad cross-neutralization ability against primary isolates from group M (subtypes A-H) and Group O. Viruses with R5, X4, and R5X4 co-receptor usage were all represented in the test panel. Kinetics of neutralization showed that NAb responses detected using a PBMC assay with a short incubation period could be lost upon extended culture. No preincubation with Ab was needed to see some inhibition of virus replication, indicating that at least partial neutralization occurs post-virus binding to target cells. Donners *et al.* [2003] (**assay development**, **co-receptor**, **kinetics**, **inter-clade comparisons**, **assay standardization/improvement**)

No. 925
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Research Contact Rebeca Geffin, Miami School of Medicine
References Geffin *et al.* 2003
Keywords autologous responses, escape, rate of progression, responses in children

- A longitudinal study of NAb responses in perinatally HIV-1 infected infants and children was undertaken, including 7 with rapid progression (RP) and 9 who did not progress rapidly (NRP). A subset of both RPs and NRPs had some plasma samples that could neutralize contemporaneous autologous viral isolates after 6 months of age, but most isolates could not be neutralized by contemporaneous plasma, only by later samples. The non-contemporaneous NAbs would persist for years, had highest titers against earlier isolates, and tended to be more potent in NRP children. This study indicates that there is ongoing NAb escape in HIV-1 + children. No correlation between HIV RNA levels and Ab production was established, although this might have been complicated by treatment. Geffin *et al.* [2003] (**autologous responses**, **escape**, **responses in children**, **rate of progression**)

No. 926
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype)
Research Contact Mascola2003b
References Mascola & Montefiori 2003
Keywords escape, review

- This paper reviews the paper by Wei *et al.* (Nature 2003) that substantiates the notion that HIV evolves to change the number and position of glycosylation sites in Envelope and this facilitates neutralization escape *in vivo*. This NAb escape mechanism is called a glycan shield. Mascola & Montefiori [2003] (**escape**, **review**)

No. 927
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing
Immunogen
Species (Isotype) macaque
References Mascola 2003
Keywords immunoprophylaxis, review

- This review dicusses the importance and function of protective antibody responses in animal model studies in the context of effective vaccine development. SHIV models have shown protection using high levels of MAbs can prevent infection, and partial protection that can influence disease course can be obtained from modest levels of NAbs. The binding properties and SHIV challenges studies conducted with infusions of combinations of MAbs b12, 2G12, and 2F5 are reviewed. Mascola [2003] (**immunoprophylaxis**, **review**)

No. 928
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: DNA prime with virus-like particle (VLP) boost, fowlpoxvirus prime with virus-like particle (VLP) boost *Strain:* B clade 89.6P *HIV component:* Env
Species (Isotype) rabbit
References Radaelli *et al.* 2003
Keywords Th1, Th2

- Three different immunization protocols using two recombinant fowlpox (FP) constructs and two expression plasmids (SIV mac239 gg/pol or HIV-1 env 89.6P) for priming and VLP particles for boosting were tested for their ability to elicit neutralizing Ab and cell-mediated immune responses. NAb responses against SHIV 89.6P were elicited in all protocols tested. Plasmid DNA (pcDNA3gag/pl SIV) was more efficient than the FP vector (FPgag/polSIV) in inducing Ab responses to the gag core protein (p27). DNA plasmid followed by a VLP boost elicited a Th0 profile. Radaelli *et al.* [2003] (**Th1**, **Th2**)

No. 929
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype B, CRF01_AE
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Polonis *et al.* 2003
Country Thailand
Keywords co-receptor, escape, inter-clade comparisons

- Neutralization of 49 subtype E HIV-1 isolates from various stages of disease and 21 subtype B viruses was compared using polyclonal Ab pools and single subtype E plasmas. Non-syncytium-inducing (NSI) CRF01 (subtype E) HIV-1 isolates showed increased sensitivity to neutralization (42%) than syncytium-inducing (SI) subtype E isolates (9%). In contrast, the viral phenotype of subtype B isolates did not correlate with neutralizaiton sensitivity. SI viruses were primarily X4 (one X4R5 was identified), NSI were R5. Low CD4+ T cell numbers in subtype E infected patients correlated with concurrent isolate resistance to neutralizing Ab responses. Polonis *et al.* [2003] (**co-receptor**, **escape**, **inter-clade comparisons**)

No. 930
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade W61D *HIV component:* gp120, Nef, Tat *Adjuvant:* AS02A (oil-in-water emulsion, 3D-monophosphoryl lipid A, QS21), AS06 (CpG, aluminum hydroxide)
Species (Isotype) macaque (IgG)
References Voss *et al.* 2003
Keywords adjuvant comparison, variant cross-recognition or cross-neutralization

- Monkeys were immunized with different combinations of gp120/NefTat/SIV-Tat three times over a three-month time period and intravenously challenged with SHIV 89.6P four weeks after the last immunzation. Vaccination induced anti-Tat, -Nef and -gp120 Ab responses that decreased until challenge. Neutralizing Ab responses against HIV-1 MN and HIV-1 W61D were observed. Vaccination with the combination of all three proteins reduced viral load and kept animals from a CD4+ T cell decline, preventing AIDS for more than 2.5 years. The adjuvant AS02A elicited NAbs and protected from disease, while AS06 did not. gp120 alone or TatNef/SIV-Tat without gp120 could not protect from disease. Voss *et al.* [2003] (**adjuvant comparison**, **variant cross-recognition or cross-neutralization**)

No. 931
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Adjuvant:* QS21
Species (Isotype) mouse
References Cunto-Amesty *et al.* 2001
Keywords mimotopes, vaccine antigen design

- Concanavalin A binds to mannose/glucose, and binds to HIV-1. Con A was used to select peptide mimics of carbohydrates that bound to Con A, and the mimetic peptides were then used for BALB/c mouse immunization. Abs raised against the mimetic peptides binds to HIV+ cells, and could weakly neutralize T cell lab adapted strains. Cunto-Amesty *et al.* [2001] (**mimotopes**, **vaccine antigen design**)

No. 932
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: E. Coli recombinant protein *HIV component:* gp120, gp41 *Adjuvant:* Complete Freund's Adjuvant (CFA), Incomplete Freund's Adjuvant (IFA)
Species (Isotype) mouse
References Li *et al.* 2002
Keywords vaccine antigen design

- A polyepitope vaccine was designed based on a recombinant GST fusion protein containing three repeats of the 2F5 core epitope ELDKWA combined with the V3 region peptide GPGRAFY. Abs raised in mice could recognize the peptides, sgp41, and CHO-WT cells that expressed HIV-1 Env on their surface. Li *et al.* [2002] (**vaccine antigen design**)

No. 933
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Montefiori *et al.* 2003
Keywords acute infection, autologous responses, escape

- AC10 is a subject who was given treatment early after infection, and had a viral rebound after cessation of therapy, which then declined to a low level. The polyclonal sera from AC10 could potently neutralize the rebound virus, and NAb escape followed with a neutralizing response against the escape variant and subsequent escape from that response. Viral loads remained low in this subject despite escape. The rebound isolate that was potently neutralized by autologous sera was not particularly neutralization sensitive, as it resisted neutralization by sCD4 and MAbs IgG1b12, 2G12 and 2F5, and was only moderately sensitive to sera from other HIV+ individuals that had high titers of NAbs to TCLA strains. Montefiori *et al.* [2003] (**autologous responses**, **acute infection**, **escape**)

No. 934
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (DH012)
Epitope
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein
Species (Isotype) chimpanzee
References Zhu *et al.* 2003
Keywords vaccine-specific epitope characteristics

- This study compares the immunogenicity of the HIV DH012 strain in chimpanzees during a natural infection with DH012 vaccinations. Naturally infected chimpanzees have sera containing potent anti-DH012 neutralization Abs, but the primary epitope is a discontinuous conformational epitope called CEV that involves the V1/V2 region, the bridging sheet, and the V3 loop. Abs that are raised upon gp120 vaccination, in contrast, are primarily against V3. DH012 has preserved the epitopes for the MAbs IgG1b12, 2G12, 17b, however natural DH012 infection in chimpanzees and DH012 gp120 vaccination in

guinea pigs does not give rise to Abs against these epitopes. Zhu *et al.* [2003] (**vaccine-specific epitope characteristics**)

No. 935
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing yes
Immunogen HIV-1 infection
Species (Isotype) human
References Aasa-Chapman *et al.* 2004
Keywords acute infection, autologous responses

- Neutralizing Ab responses to autologous virus envelopes were studied in four acutely HIV-1 infected, treatment-naive, homosexual men (MM1,MM2, MM4 and MM8). Detection of gp120 antibodies was rapid using ELISPOT, within a few weeks, but detection of neutralizing antibodies took between 3 and 16 months, precluding involvement of detectable NAbs with resolution of viremia. Heterologous NAb responses arose even later, by 3 months or more, suggesting gradual broadening of the immune response. Aasa-Chapman *et al.* [2004] (**autologous responses**, **acute infection**)

No. 936
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (V3) (IIIB)
Epitope
Subtype B
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB, B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA), Incomplete Freund's Adjuvant (IFA)
Species (Isotype) rabbit, guinea pig
References Berman *et al.* 1992
Keywords vaccine-specific epitope characteristics

- Abs derived from immunizations of rabbits and guinea pigs with either IIIB- or MN-gp120 were compared. Both could block gp120 binding to CD4, and this activity was strain-specific. Antisera from IIIB-rgp120 immunizations could only neutralize displayed homologous virus, while sera from MN-rgp120 rabbit vaccinations could neutralize MN 3/8 additional tested viruses. Berman *et al.* [1992] (**vaccine-specific epitope characteristics**)

No. 937
MAb ID polyclonal
HXB2 Location Env
Author Location Env (YU-2)
Epitope
Subtype B
Neutralizing yes
Immunogen Vaccine
Vector/Type: DNA with CMV promotor, DNA prime with protein boost *Strain:* B clade YU2 *HIV component:* gp140 *Adjuvant:* monophosphoryl lipid A, trehalose dicorynomycolate
Species (Isotype) mouse (IgG)
References Bower *et al.* 2004
Keywords adjuvant comparison, vaccine antigen design

- DNA vaccines encoding an uncleaved form of YU-2 gp140 stabilized with a synthetic trimerization domain isolated from the fibritin (FT) protein of the T4 bacteriophage and fused to murine C3d as a molecular adjuvant, could induce low titers of neutralizing antibodies against primary isolates HIV-1 YU-2 and HIV-1 ADA. DNA was administered by gene gun immunization to BALB/c mice, protein boost was performed by intraperitoneal injection. C3d is a component of the innate immune system that can serve as a moelcular adjuvant and had been previously shown to enhance immunogenicity. Bower *et al.* [2004] (**adjuvant comparison**, **vaccine antigen design**)

No. 938
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Subtype multiple
Neutralizing N
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB, A clade UG37, B clade HAN2, D clade UG21, F clade BR29 *HIV component:* gp140, gp120ΔV1, V2, and V3 *Adjuvant:* Complete Freund's Adjuvant (CFA), Incomplete Freund's Adjuvant (IFA)
Species (Isotype) rabbit
References Jeffs *et al.* 2004
Keywords inter-clade comparisons, vaccine antigen design

- A set of oligomeric envelope proteins were made from six primary isolates for potenial use as vaccine antigens: 92/UG/037 (clade A), HAN2/2 (clade B), 92/BR25/025 (clade C), 92/UG/021 (clade D), 93/BR/029 (clade F) and MVP5180 (clade O). This was one of a panel of MAbs used to explore folding and exposure of well characterized epitopes. The clade C isolate BR25 is apparently misfolded, as conformation-dependent antibodies did not bind to it. Polyclonal sera raised in rabbits against the A, B, D and F antigens, which were deemed pure enough for immunization, as well as IIIB and IIIB with the V1, V2 and V3 loops deleted, cross-bound the other antigens, so shared epitopes across clades, but none of the sera had neutralizing activity. Jeffs *et al.* [2004] (**vaccine antigen design**, **inter-clade comparisons**)

No. 939
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Subtype B, CRF01_AE
Neutralizing

Immunogen HIV-1 infection, Vaccine
Vector/Type: protein *Strain:* B clade MN, B clade GNE8, E clade CM244 *HIV component:* gp120 *Adjuvant:* aluminum hydroxide
Species (Isotype) human
References Lee *et al.* 2001
Keywords assay development, inter-clade comparisons, vaccine antigen design, vaccine-induced epitopes

- An assay was developed that characterizes antibody binding to primary isolates, and using this system there was a correlation between binding activity and neutralization by sera from HIV-infected people and gp120 vaccinated individuals. The magnitude and breadth of oligomeric, cell surface gp120 binding Abs induced by HIV-1 subtype B vaccines was characterized. The responses in people vaccinated with mono- and bivalent rgp120 vaccines (AIDSVAX B and AIDSVAX B/B AIDSVAX B/E) indicated that increasing the number of antigens increased the cross-binding activities, in support of polyvalent vaccines. Lee *et al.* [2001] (**assay development**, **vaccine antigen design**, **vaccine-induced epitopes**, **inter-clade comparisons**)

No. 940
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: gp120-MAb A32 complex *Strain:* B clade 89.6, B clade BaL *HIV component:* gp120-Mab complex *Adjuvant:* Cholera toxin (CT), Complete Freund's Adjuvant (CFA), Incomplete Freund's Adjuvant (IFA), Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) guinea pig
References Liao *et al.* 2004
Keywords vaccine antigen design

- A32-rgp120 complexes opened up the CCR5 co-receptor binding site, but did not induce neutralizing antibodies with greater breadth among B subtype isolates than did uncomplexed rgp120 in vaccinated guinea pigs. The vaccine that gave the greatest breadth comparing A32-rgp120 BaL, A32-rgp120 89.6, rgp120 BaL, and rgp120 89.6, was the uncomplexed rgp120 BaL, as it neutralized 9/14 B clade isolates tested (60%). Liao *et al.* [2004] (**vaccine antigen design**)

No. 941
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (JRFL)
Epitope
Subtype B
Neutralizing yes
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade JRFL *HIV component:* gp120 *Adjuvant:* C3d fusion
Species (Isotype) humanized mouse (IgG)
References Liu *et al.* 2004
Keywords adjuvant comparison

- BALB/c mice were immunized with codon-optimized or C3d-fused DNA vaccine constructs and analyzed for their ability to elicit humoral and cell-mediated immune responses. Each strategy increased binding and gave rise to earlier appearance of neutralizing antibody respones against IIIB and MN viruses, but the combination did not act synergistcally. C3d and codon optimization also gave enhanced CD8+ T cell responses to the epitope SIHIGPGRAFYTTGE. Liu *et al.* [2004] (**adjuvant comparison**)

No. 942
MAb ID polyclonal
HXB2 Location Env
Author Location Env (SF2)
Epitope
Subtype multiple
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF2 *HIV component:* gp120 *Adjuvant:* aluminum hydroxide, Incomplete Freund's Adjuvant (IFA), MF59, Other
Species (Isotype) baboon
References Haigwood *et al.* 1992
Keywords adjuvant comparison, vaccine antigen design, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization

- Baboons were given intramuscular immunization with env 2-3 SF2 (aa Ile-26 to Ala-510) or rgp120SF2. Native, glycosylated rgp120 SF2, gave a broader range of heterologous neutralizing Ab responses than denatured, non-glycosylated env 2-3 SF2. Repeated immunizations with the native rgp120 gave rise to weak but detectable NAbs against two African strains, NDK and ZR6. IFA/MTP-PE gave the highest titer antibodies.of many adjuvant combinations tested. Haigwood *et al.* [1992] (**adjuvant comparison**, **vaccine antigen design**, **variant cross-recognition or cross-neutralization**, **vaccine-specific epitope characteristics**)

No. 943
MAb ID polyclonal
HXB2 Location Env
Author Location Env (89.6)
Epitope
Subtype B
Neutralizing yes
Immunogen Vaccine
Strain: B clade 89.6 *HIV component:* gp140, gp160, gp160ΔV3, gp140ΔV3
Species (Isotype) macaque, mouse
References Lorin *et al.* 2004
Keywords vaccine antigen design, variant cross-recognition or cross-neutralization

- Mice susceptible to MV infection were intraperitoneally immunized with native HIV-1 89.6 env gp160 and gp140 and δV3 HIV-1 89.6 mutants expressed in live attenuated Schwarz measles vector (MV). The gp160ΔV3 construct raised more cross-reactive NAbs to primary isolates than did native gp160, and sera from the gp160ΔV3 animals neutralized SHIV 89.6, clade B strains Bx09, 92US660 and 92US714, and clade A virus 3253 but not to clade B 92HT593, at a 1:30 dilution. A HIVIG/2F5/2G12 combination was used as a positive control and could neutralize all isolates. The vaccine constructs had an additional 2F5 MAb epitope, ELDKWAS, but responses were not directed towards this epitope. Mice and macaques could raise anti-HIV responses in mice and macaques with pre-existing MV immunity. Lorin *et al.* [2004] (**vaccine antigen design**, **variant cross-recognition or cross-neutralization**)

No. 944
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References McCaffrey *et al.* 2004
Keywords antibody binding site definition and exposure, vaccine antigen design

- Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The loss of the glycan within the V3 loop (GM299 V3) and adjacnt to the C-terminal end of the V3 loop (GM329 C3) increased neutralization susceptibility to both sera, but the loss of sites in C2, C4, and V5 did not alter neutralization susceptibility. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 945
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (HXBc2)
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: Con A-NS *Strain:* B clade HXBc2 *HIV component:* Env
Species (Isotype) macaque (IgA, IgG)
References Miyake *et al.* 2004
Keywords genital and mucosal immunity

- Intranasal immunizations of three macaques with SHIV-nanospheres (SHIV-NS) induced vaginal anti-HIV-1 gp120 IgA and IgG antibodies. After intra-vaginal challenge with SHIV KU-2, 1/3 control animals and 1/3 SHIV vaccinated animals were infected, but the SHIV vaccinated animals had low viral loads that fell to undetectable levels. After intravenous re-challenge, all animals were infected, but SHIV immunized animals had lower viral loads. Miyake *et al.* [2004] (**genital and mucosal immunity**)

No. 946
MAb ID polyclonal
HXB2 Location Env
Author Location gp41 (HXB2)
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
References Opalka *et al.* 2004
Keywords assay development, assay standardization/improvement

- An antigen panel representing different regions of gp41 was generated, and sera from 23 individuals were screened. Anti-gp41 titers were very high, and sera bound to many regions of gp41, there were no immunologically silent regions. Many individuals had broad responses to diverse regions. High titer responses tended to focus on the N-heptad, C-heptad and 2F5-4E10 regions, but there was no correlation between neutralization capacity of sera and the particular peptides recognized. Opalka *et al.* [2004] (**assay development**, **assay standardization/improvement**)

No. 947
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Research Contact Abraham Pinter, Public Health Research Institute, Newark, NJ, 07103. pinter@phri.o
References Pinter *et al.* 2004
Country United States
Keywords variant cross-recognition or cross-neutralization

- V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. 28 sera were tested – 24/28 sera gave greater than 90% neutralization of SF162 at dilutions of 1:180, while only 2/28 could give 90% neutralization of JRFL, and only 9/28 gave 50% neutralization at dilutions of 1:180. A chimera with SF162 V1V2 in a JRFL Env backbone was neutralization sensitive to most sera at a comparable level to SF162 Env, and in some cases the JRFL-SF162 V1V2 chimera was even more sensitive than JRFL. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)

No. 948
MAb ID polyclonal
HXB2 Location Env
Author Location Env (gp160)
Epitope
Subtype multiple
Neutralizing
Immunogen Vaccine
Vector/Type: DNA, DNA prime with protein boost *Strain:* B clade LAI, A clade 92UG031, C clade 92BR025 *HIV component:* gp160 *Adjuvant:* GM-CSF
Species (Isotype) mouse (IgG)
References Rollman *et al.* 2004
Keywords adjuvant comparison, enhancing activity, Th1, Th2, vaccine antigen design, variant cross-recognition or cross-neutralization

- Vaccination of mice with subtype B Env raised antibodies primarily against subtype B alone, while A+B+C clade Envs raised antibodies that could neutralize the autologous B, C strains, and weakly neutralize the A strain. Serum IgG responses to gp120s including all gp120 variable regions were induced in animals vaccinated with subtypes A, B and C of HIV-1 gp160 with rGM-CSF as adjuvant. Boosting with rgp160 with CpG-ODN enhanced IgG responses, shifted the Th1/Th2 to be more balanced, and these animals made both IgG and Ig2a responses and had expanded recognition of constant regions. The B clade vaccine was LAI, and the A and C clade vaccines were actually V1-V5 of the A and C strains cloned into a LAI backbone. gp41 peptides were also recognized by sera. T cell responses to the multi-clade vaccine had enhanced cross-reactive CD4 T-cell proliferative responses, but diminished gamma IFN CD8 T-cell responses. Rollman *et al.* [2004] (**adjuvant comparison**, **enhancing activity**, **vaccine antigen design**, **variant cross-recognition or cross-neutralization**, **Th1**, **Th2**)

No. 949
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* C3d fusion
Species (Isotype) mouse (IgG, IgG2a)
References Toapanta & Ross 2004
Keywords adjuvant comparison, Th1, Th2

- Mice [C57BL/6 (H-2b), BALB/c (H-2d), C3H/H3 (H-2k) and CD-1 Swiss] were vaccinated DNA carrying with 2 or 3 complement C3d genes fused to secreted sgp120. Responses were enhanced with C3d, particularly in outbred mice. sgp120-C3d-DNA vaccination induced a primarily IgG1 anti-Env Ab response in inbred mouse strains, while outbred mice had mixed IgG1/IgG2a responses; similarly IL4 (Th2) T-cell responses were observed in inbred mice, and mixed IL4 and IFN gamma (Th1/Th2) responses were observed in outbred mice. An increased avidity maturation of anti-Env Abs in outbred mice was also observed. Toapanta & Ross [2004] (**adjuvant comparison**, **Th1**, **Th2**)

No. 950
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, Protease
Species (Isotype) human (IgA, IgG)
References Wright *et al.* 2004
Keywords genital and mucosal immunity, vaccine antigen design

- HIV-1 specific responses were seldom detected after systemic or mucosal vaccination with HIV gp120 in a canarypox vector with a rgp120 boost. A limited IgA and CTL response was observed after rectal vaccination, but overall, canary pox virus was not an effective mucosal immunogen. Wright *et al.* [2004] (**genital and mucosal immunity**, **vaccine antigen design**)

No. 951
MAb ID polyclonal
HXB2 Location Env
Author Location Env (735–752)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) human, rabbit
References Kennedy *et al.* 1986
Keywords assay standardization/improvement

- Rabbits intramusculary immunized with peptide KLH ("HTLV-III aa 735-752") produced peptide-specific, serum Ab responses. In an ELISA, AIDS patient derived antisera tested positive for gp41-specific Ab. Kennedy *et al.* [1986] (**assay standardization/improvement**)

No. 952
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Neutralizing
Immunogen HIV-1 infection, Vaccine

Species (Isotype) human
References Zolla-Pazner 2004
Keywords review, vaccine antigen design

- This review summarizes neutralizing epitopes on Env and their use as vaccine antigens. Most antibodies are not neutralizing, and while some antibodies directed to conserved domains can neutralize the virus, these are generally poorly immunogenic. Variable loops do not elicit much cross-reactive neutralization, although the stem regions of these loops are more conserved so may have some promise. Polyclonal pooled sera from infected people can generally neutralize heterologous virus, suggesting that neutralizing epitopes are yet to be discovered. Polyvalent vaccine design is considered key. Zolla-Pazner [2004] (**vaccine antigen design**, **review**)

No. 953
MAb ID polyclonal
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Adjuvant:* gp41 N-HR and C-HR helical peptides
Species (Isotype) rabbit (IgG)
Ab Type C-HR, N-HR, six-helix bundle
References Golding *et al.* 2002b; de Rosny *et al.* 2001

- The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter anti-C-HR Abs inability to inhibit fusion. Golding *et al.* [2002b]
- A panel of Abs against gp41 heptad repeats N-HR, C-HR, and self-assembled stable N-HR and C-HR six helix bundles were generated. de Rosny *et al.* [2001]

No. 954
MAb ID 101-342
HXB2 Location Env
Author Location gp120 (476–505 HAM112, O group)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* O group HAM112 *HIV component:* gp160
Species (Isotype) mouse (IgG2aκ)
Ab Type C-term
References Scheffel *et al.* 1999

- 101-342: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity. Scheffel *et al.* [1999]

No. 955
MAb ID 101-451
HXB2 Location Env
Author Location gp120 (498–527 HAM112, O group)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* O group HAM112 *HIV component:* gp160
Species (Isotype) mouse (IgG2bκ)
Ab Type C-term
References Scheffel *et al.* 1999

- 101-451: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity. Scheffel *et al.* [1999]

No. 956
MAb ID 120-1
HXB2 Location Env
Author Location gp120 (503–532)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: peptide
Species (Isotype) mouse (IgMκ)
Ab Type C-term
References Dalgleish *et al.* 1988; Chanh *et al.* 1986

No. 957
MAb ID T26
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein
Species (Isotype) mouse
Ab Type C-term
Research Contact Patricia Earl, National Institute of Allergy and Infectious Diseases
References Kilgore *et al.* 2003; Earl *et al.* 1997; Earl *et al.* 1994
Keywords antibody binding site definition and exposure, antibody generation, variant cross-recognition or cross-neutralization

- T26: Mab is restricted in its binding to gp41 of the LAI isolate and not to gp41 of the MN, Ada and RF isolates. Antibody specificity may be determined by LAI residues D637E, N641D and H648Y. T26 binds to the N-terminal half of the C helix (aa630-680) of the LAI envelope, specifically targeting a conformational epitope within the six-helix bundle of gp41. Addition of the C-helical peptide inhibitor from LAI (T26 reactive) rescued the binding activity of MAb T26 to cell-surface expressed RF envelope (T26 non-reactive) triggered with sCD4 or cell-surface expressed receptors in a surface immunoprecipitation assay. This supports that C-peptide entry inhibitors bind to the gp41 N-helical coiled-coil, disrupting native six-helix bundles. Kilgore *et al.* [2003] (**antibody binding site definition and exposure**)
- T26: T26 was raised against the gp140 tetramer, binds to gp41 and is a highly strain specific. Earl *et al.* [1997] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- T26: A panel of 138 MAb raised against different forms of soluble Env. Earl *et al.* [1994] (**antibody generation**)

No. 958
MAb ID D33
HXB2 Location Env
Author Location gp120 (IIIB)

Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS, C-term, N-term
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D33: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D33 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – D33 was unusual for the group of A1 MAbs, because while it blocked CD4 binding completely, but competed with MAbs that did not in a BIAcore assay – both the N- and C-terminal ends of gp120 are involved in D33 binding. Sugiura *et al.* [1999]
- D33: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 959
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgA)
Ab Type CD4BS, C-term, V3-C4
References Vincent *et al.* 2004
Country France
Keywords genital and mucosal immunity

- IgA derived from sera and saliva from 5 HIV-1 infected patients undergoing ART therapy reacted to peptide antigens corresponding to the C3-V4 region of gp120 and the C-terminal part of gp41. HIV-1-specific IgA obtained in 6/26 sera and 5/25 saliva samples inhibited gp120-sCD4 protein binding. Vincent *et al.* [2004] (**genital and mucosal immunity**)

No. 960
MAb ID 212A
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type C1
Research Contact James Robinson, Tulane University, LA
References Pantophlet *et al.* 2003b; Binley *et al.* 1998; Sullivan *et al.* 1998b; Parren *et al.* 1997b; Wyatt *et al.* 1997; Ditzel *et al.* 1997; Fouts *et al.* 1997; Binley *et al.* 1997a; Moore & Sodroski 1996; Moore *et al.* 1994d; Robinson *et al.* 1992
Keywords vaccine antigen design

- 212A: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- 212A: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- 212A: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10. Sullivan *et al.* [1998b]
- 212A: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 212A bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997]
- 212A: Does not neutralize TCLA strains or primary isolates. Parren *et al.* [1997b]
- 212A: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids are deleted. Wyatt *et al.* [1997]
- 212A: Binding enhanced by anti-V3 MAb 5G11 – reciprocal inhibition with anti-C1 MAbs. Moore & Sodroski [1996]
- 212A: Mutations that inhibit binding: C1 (45 W/S) and V5 (463 N/D) – and enhance binding: V2 (179/180 LD/DL) and C5 (495 G/K) Moore *et al.* [1994d]

No. 961
MAb ID 522-149
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) mouse
Ab Type C1
Research Contact G. Robey, Abbott Inc.
References Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Yang *et al.* 2000; Binley *et al.* 1998; Trkola *et al.* 1996a; Moore & Sodroski 1996
Keywords antibody interactions, vaccine antigen design

- 522-149: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- 522-149: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results

suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C1-binding Fab that had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)

- 522-149: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000]
- 522-149: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- 522-149: Binding is enhanced by C5 antibodies M91 and 1C1 – mutual binding-inhibition with anti-C1 antibody 133/290 – binding is destroyed by a W/L (position 61, LAI) gp120 amino acid substitution – other C1 antibodies enhance binding to gp120. Moore & Sodroski [1996]
- 522-149: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]

No. 962
MAb ID CA1 (ARP3117)
HXB2 Location Env
Author Location Env
Epitope
Subtype A
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia prime with gp120 boost
Strain: A clade *HIV component:* Env
Species (Isotype) mouse
Ab Type C1
References Jeffs *et al.* 2004
Keywords inter-clade comparisons, vaccine antigen design

- CA1: A set of oligomeric envelope proteins were made from six primary isolates for potenial use as vaccine antigens: 92/UG/037 (clade A), HAN2/2 (clade B), 92/BR25/025 (clade C), 92/UG/021 (clade D), 93/BR/029 (clade F) and MVP5180 (clade O). This was one of a panel of MAbs used to explore folding and exposure of well characterized epitopes. The clade C isolate BR25 is apparently misfolded, as conformation-dependent antibodies did not bind to it. CA1 is a MAb that binds to a linear epitope in the C1 region of gp120 that was raised against clade A variant 92/UG/029. CA1 was subtype-specific and bound only to the antigen from all clade A. Polyclonal sera raised in rabbits against these antigens cross-bound the other antigens, but none of the sera had neutralizing activity. Jeffs *et al.* [2004] (**vaccine antigen design**, **inter-clade comparisons**)

No. 963
MAb ID CA13 (ARP3119)
HXB2 Location Env
Author Location Env
Epitope
Subtype A
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia prime with gp120 boost
Strain: A clade *HIV component:* Env
Species (Isotype) mouse
Ab Type C1
References Jeffs *et al.* 2004
Keywords inter-clade comparisons, vaccine antigen design

- CA13: A set of oligomeric envelope proteins were made from six primary isolates for potenial use as vaccine antigens: 92/UG/037 (clade A), HAN2/2 (clade B), 92/BR25/025 (clade C), 92/UG/021 (clade D), 93/BR/029 (clade F) and MVP5180 (clade O). This was one of a panel of MAbs used to explore folding and exposure of well characterized epitopes. The clade C isolate BR25 is apparently misfolded, as conformation-dependent antibodies did not bind to it. CA13 is a MAb that binds to a linear epitope in the C13 region of gp120 that was raised against clade A variant 92/UG/029. C13 bound to antigens from all clades A-F, as well as group O. Polyclonal sera raised in rabbits against these antigens cross-bound the other antigens, but none of the sera had neutralizing activity. Jeffs *et al.* [2004] (**vaccine antigen design**, **inter-clade comparisons**)

No. 964
MAb ID L19
HXB2 Location Env
Author Location gp120 (HXBc2)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type C1
References Ditzel *et al.* 1997

- L19: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for the selection of Fabs – six N-term Fabs, L19 L34, L35, L52, L59, and L69, were obtained that have a similar epitope to Fab p7. Ditzel *et al.* [1997]

No. 965
MAb ID M90
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *HIV component:* Env
Species (Isotype) (IgG1)
Ab Type C1

Research Contact Fulvia di Marzo Veronese
References Pantophlet *et al.* 2003b; Yang *et al.* 2000; Binley *et al.* 1999; Binley *et al.* 1998; Wyatt *et al.* 1997; Ditzel *et al.* 1997; Moore & Sodroski 1996; DeVico *et al.* 1995; di Marzo Veronese *et al.* 1992

- M90: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b]
- M90: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000]
- M90: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999]
- M90: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- M90: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-82, are deleted. Wyatt *et al.* [1997]
- M90: Reciprocal inhibition of binding of other anti-C1 MAbs – inhibits CD4 binding site MAbs – enhances binding of V2 MAbs G3-4 and SC258. Moore & Sodroski [1996]
- M90: Reacted with both non-reduced (but not denatured) covalently cross-linked gp120-CD4 complex. DeVico *et al.* [1995]
- M90: Reactive only with native gp120, so binds to a discontinuous epitope – reacts with multiple strains. di Marzo Veronese *et al.* [1992]

No. 966
MAb ID MAG 104
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type C1
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 104: Only observed amino acid substitution that reduces binding: 88 N/P and 106 E/A – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb. Kang *et al.* [1994]

No. 967
MAb ID MAG 45 (#45)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type C1
Research Contact C. Y. Kang, IDEC Inc
References Yang *et al.* 2000; Wyatt *et al.* 1997; Moore & Sodroski 1996; Kang *et al.* 1994

- MAG 45: Called #45 – a combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000]
- MAG 45: Called #45 – binds to efficiently sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-50, are deleted. Wyatt *et al.* [1997]
- MAG 45: Reciprocal binding inhibition with anti-C1-C5 and anti-C1-C4 discontinuous MAbs – binding enhanced by anti-V3 5G11 – inhibits binding of anti-CD4 binding site MAbs. Moore & Sodroski [1996]

- MAG 45: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb. Kang *et al.* [1994]

No. 968
MAb ID MAG 95
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type C1
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 95: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb. Kang *et al.* [1994]

No. 969
MAb ID MAG 97
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type C1
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 97: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb. Kang *et al.* [1994]

No. 970
MAb ID P35
HXB2 Location Env
Author Location Env
Epitope
Neutralizing
Immunogen
Species (Isotype) human
Ab Type C1
References Zwick *et al.* 2003; Kwong *et al.* 2002
Keywords antibody binding site definition and exposure, antibody interactions

- P35: called p35. scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restrict CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C1-binding Fab with a discontinuous epitope that had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)
- P35:Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-terminal, linear. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)

No. 971
MAb ID T9
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen Vaccine
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type C1
Research Contact Patricia Earl and Christopher Broder, NIH
References Golding *et al.* 2002b; Earl *et al.* 1997; Broder *et al.* 1994
Keywords antibody binding site definition and exposure, antibody generation, variant cross-recognition or cross-neutralization

- There are two HIV-Abs with the name T9, one binds to gp41, one to gp120.
- T9: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b – nor did it alter two gp41 MAbs, T9 and D61, inability to inhibit fusion. Golding *et al.* [2002b] (**antibody binding site definition and exposure**)
- T9: This antibody, along with 7 others (M10, D41, D54, T6, T4, T10 and T35), can block the linear murine MAb D61, and the human MAb 246-D, which both bind to the immunodominant region near the two Cys in gp41 – most of these antibodies are

oligomer dependent – all of the MAbs are reactive with ten different HIV-1 strains – members of this competition group are blocked by sera from HIV-1 + individuals. Earl *et al.* [1997] (**antibody binding site definition and exposure**)

- T9: One of five MAbs (T4, T6, T9, T10 and T35) in a competition group that bind to a conformation-dependent epitope in gp41 and is oligomer specific – neutralizes IIIB and SF2. Broder *et al.* [1994] (**antibody generation**, **variant cross-recognition or cross-neutralization**)

No. 972
MAb ID p7
HXB2 Location Env
Author Location gp120 (HXBc2)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type C1
References Parren *et al.* 1997b; Ditzel *et al.* 1997

- p7: gp120 immobilized on solid phase by capture with sCD4 was used for selection of Fabs – three novel N-term Fabs were obtained that bind to similar epitopes, p7, p20, and p35 – a C1 W/S substitution at position 45 abolished binding, a Y/D at position 45 reduced binding, and C5 region substitutions 475 M/S and 493 P/K enhanced binding – compete with MAbs M85, M90 and 212A, but not M91 and G3-299. Ditzel *et al.* [1997]
- p7: Does not neutralize TCLA strains or primary isolates. Parren *et al.* [1997b]

No. 973
MAb ID L100
HXB2 Location Env
Author Location gp120 (HXBc2)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type C1-C2
References Kwong *et al.* 2002; Parren & Burton 1997; Parren *et al.* 1997b; Ditzel *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation, variant cross-recognition or cross-neutralization

- L100: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-terminal, discontinuous. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- L100: gp120 immobilized on solid phase by capture with sCD4 and then masked with Fab p7 allowed selection of a new Fab, L100, with a novel specificity for C1 and C2 – gp120 C1 substitutions 69 W/L and 76 P/Y abolish L100 binding, and C2 substitutions 252 R/W, 256 S/Y, 262 N/T and 267 E/L abolish or strongly inhibit L100 binding – inhibits binding of MAbs M90 and G3-299, but not M85, 212A, and M91. Ditzel *et al.* [1997]; Parren & Burton [1997] (**antibody binding site definition and exposure**, **antibody generation**)
- L100: Does not neutralize TCLA strains or primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)

No. 974
MAb ID 2/11c (211c, 2.11c, 211/c, 2-11c)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (weak)
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type C1-C4
Research Contact James Robinson, Tulane University, LA
References Kwong *et al.* 2002; Xiang *et al.* 2002a; Binley *et al.* 1998; Wyatt *et al.* 1997; Li *et al.* 1997; Fouts *et al.* 1997; Binley *et al.* 1997a; Trkola *et al.* 1996a; Moore & Sodroski 1996
Keywords antibody binding site definition and exposure

- 2/11c: Called 211/c. Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-terminus, discontinuous. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)

- 2/11c: Used as a negative control in a study of CD4i MAbs. Xiang *et al.* [2002a]
- 2/11c: Called 211/c – a panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998]
- 2/11c: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – 2/11c bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997]
- 2/11c: Called 2.11c – One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 67 mug/ml. Li *et al.* [1997]
- 2/11c: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-74, are deleted. Wyatt *et al.* [1997]
- 2/11c: Inhibits binding of anti-C1, -C5, -C4, -V3 and anti-CD4 binding site MAbs – induces binding of some anti-V2 and CD4i MAbs (48d and 17b) – similar reactivity pattern to A32, but less cross-reactive and lower affinity – A32 and 211/c are unique among known human and rodent MAbs. Moore & Sodroski [1996]
- 2/11c: Called 211c – does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]

No. 975
MAb ID A32
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type C1-C4, CD4i
Research Contact James Robinson, Tulane University, New Orleans, LA, USA
References Liao *et al.* 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Kwong *et al.* 2002; Grundner *et al.* 2002; Yang *et al.* 2002; Finnegan *et al.* 2001; Yang *et al.* 2000; Binley *et al.* 1999; Binley *et al.* 1998; Sullivan *et al.* 1998b; Parren *et al.* 1997b; Boots *et al.* 1997; Wyatt *et al.* 1997; Burton & Montefiori 1997; Fouts *et al.* 1997; Binley *et al.* 1997a; Trkola *et al.* 1996a; Wu *et al.* 1996; Moore & Sodroski 1996; Moore & Ho 1995; Wyatt *et al.* 1995; Moore *et al.* 1994b
Keywords antibody binding site definition and exposure, antibody interactions, co-receptor, interclade comparisons, mimotopes, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- A32: A32-rgp120 complexes opened up the CCR5 co-receptor binding site, but did not induce neutralizing antibodies with greater breadth among B subtype isolates than did uncomplexed rgp120 in vaccinated guinea pigs. Liao *et al.* [2004] (**vaccine antigen design**)
- A32: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- A32: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. A32 is described as having a C1-C4 discontinuous CD4i epitope, and had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)
- A32: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface – non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12 – the MAb 17b was sCD4 inducible on gp160deltaCT PL. Grundner *et al.* [2002] (**vaccine antigen design**)
- A32: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-terminal, discontinuous. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)

- A32: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002] (**antibody binding site definition and exposure**)
- A32: Using a cell-fusion system, it was found CD4i antibodies 17b, 48d, and CG10 reacted faintly with Env expressing HeLA cells even in the absence of sCD4 or CD4 expressing target cells. Reactivity increased after sCD4 addition, but not after CD4 expressing target cell addition, and binding was not increased at the cell-to-cell CD4-Env interface. This suggests the CD4i co-receptor binding domain is largely blocked at the cell-fusion interface, and so CD4i antibodies would not be able access this site and neutralize cell-mediated viral entry. However, CD4i MAbs 8F101 and A32, that bind outside the co-receptor domain, had a different pattern. They reacted after the formation of gp120-CD4-CXCR4 tri-complexes, so co-receptor interactions allowed exposure of their epitopes. Finnegan *et al.* [2001] (**antibody binding site definition and exposure**)
- A32: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000] (**vaccine antigen design**)
- A32: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999] (**antibody binding site definition and exposure**)
- A32: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. Binley *et al.* [1998] (**antibody binding site definition and exposure**)
- A32: Enhances binding of CD4i MAbs 17b and 48d, and a MAb generated in response to gp120-CD4 complex, CG10. Sullivan *et al.* [1998b] (**antibody interactions**)
- A32: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – A32 has a unique epitope involving mostly C2 but C1 and C4 contribute – six quite variable phage inserts were recognized, with a consensus of LPWYN – a central Trp was the most conserved element, consistent with W427 being an important residue for binding gp120. Boots *et al.* [1997] (**antibody binding site definition and exposure**, **mimotopes**)
- A32: Review. Burton & Montefiori [1997] (**review**)
- A32: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – A32 bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- A32: Does not neutralize TCLA strains or primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- A32: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding. Wyatt *et al.* [1997] (**antibody binding site definition and exposure**)
- A32: Reciprocal inhibition of binding of anti-C1, -C5, -C4, -V3 and anti-CD4 binding site MAbs – induces binding of some anti-V2 and sCD4 inducible MAbs (48d and 17b) – very similar competition pattern between 2/11c, A32 and 211/c are unique among known human and rodent MAbs. Moore & Sodroski [1996] (**antibody binding site definition and exposure**, **antibody interactions**)
- A32: Does not neutralize JR-FL, or any strain strongly – partial inhibition of gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a] (**co-receptor**)
- A32: Not neutralizing – binds domains that interact with gp41 – MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 and binding of A32 does not block this inhibition. Wu *et al.* [1996] (**antibody binding site definition and exposure**)
- A32: Review: epitope is distinct from CD4BS MAbs, 48d and 17b, and 2G12. Moore & Ho [1995] (**antibody binding site definition and exposure**)
- A32: Epitope is better exposed upon CD4 binding to gp120 – binding of A32 enhances binding of 48d and 17b – studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 48d in the presence sCD4 involves the V1/V2 loops, with more significant involvement of V2. Wyatt *et al.* [1995] (**antibody binding site definition and exposure**, **antibody interactions**)
- A32: Reacted with virtually every gp120 monomer of every clade tested, most conserved gp120 monomer epitope known. Moore *et al.* [1994b] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 976
MAb ID C11 (c11)
HXB2 Location Env
Author Location gp120

Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type C1-C5
Research Contact James Robinson, Tulane University, LA
References Pantophlet *et al.* 2003b; Ohagen *et al.* 2003; Raja *et al.* 2003; Kwong *et al.* 2002; Basmaciogullari *et al.* 2002; Grundner *et al.* 2002; Yang *et al.* 2002; Binley *et al.* 1999; Sullivan *et al.* 1998b; Parren *et al.* 1997b; Wyatt *et al.* 1997; Fouts *et al.* 1997; Binley *et al.* 1997a; Wu *et al.* 1996; Trkola *et al.* 1996a; Moore & Sodroski 1996; Moore *et al.* 1994d; Robinson *et al.* 1992
Keywords antibody binding site definition and exposure, antibody interactions, brain/CSF, co-receptor, vaccine antigen design, variant cross-recognition or cross-neutralization

- C11: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. C11 recognized most variants,some from each of the four individuals, by gp120 immunoprecipitation. Ohagen *et al.* [2003] (**brain/CSF**, **variant cross-recognition or cross-neutralization**)
- C11: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- C11: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. C11 was used as a negative control, as C11 binding did not alter binding of CD4-independent gp120 to CCR5, nor binding to CCR5-expressing Cf2Th cells. Raja *et al.* [2003] (**co-receptor**)
- C11: gp120 mutants were used to define the CXCR4 binding site using CXCR4 displayed on paramagnetic proteoliposomes (PMPLs) to reduce non-specific gp120 binding – basic residues in the V3 loop and the beta19 strand (RIKQ, positions 419-422) were involved, and deletion of the V1-V2 loops allowed CD4-independent CXCR4 binding – MAbs 17b (CD4i) and F105 (CD4BS) were used to study conformational changes in the mutants – C11 was used to detect gp120 binding to CXCR4 or CCR5 on PMPLs. Basmaciogullari *et al.* [2002] (**antibody binding site definition and exposure**)
- C11: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface – non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12 – the MAb 17b was sCD4 inducible on gp160deltaCT PL. Grundner *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- C11: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-term and C-term binding. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- C11: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002] (**antibody binding site definition and exposure**)
- C11: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999] (**vaccine antigen**

design)
- C11: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10. Sullivan *et al.* [1998b] (**antibody interactions**)
- C11: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – C11 bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- C11: Does not neutralize TCLA strains or primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- C11: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – partial re-exposure if sCD4 was bound – does not bind to HXBc2 gp120 if the 19 C-term amino acids are deleted. Wyatt *et al.* [1997] (**antibody binding site definition and exposure**)
- C11: Binding enhanced by anti-V3 MAb 5G11 – reciprocal inhibition with anti-C1 MAbs. Moore & Sodroski [1996] (**antibody interactions**)
- C11: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a] (**antibody binding site definition and exposure**)
- C11: Did not block ability of gp120-sCD4 complexes to inhibit MIP-1alpha binding – binds to gp41-binding domain. Wu *et al.* [1996] (**antibody binding site definition and exposure**)
- C11: Mutations that inhibit binding: C1 (45 W/S, 88 N/P) – V5 (463 N/D) – and C5 (491 I/F, 493 P/K and 495 G/K) and enhance binding: C1 (36 V/L) – V1-V2 (152/153 GE/SM) – and DeltaV1/V2/V3. Moore *et al.* [1994d] (**antibody binding site definition and exposure**)

No. 977
MAb ID L81
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type C1-C5
References Parren *et al.* 1997b; Ditzel *et al.* 1997

- L81: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – L81 binding is abolished by C1 substitution 45 W/S, C5 substitution 491 I/F, and C3 substitution L/A. Ditzel *et al.* [1997]
- L81: Does not neutralize TCLA strains or primary isolates. Parren *et al.* [1997b]

No. 978
MAb ID B2C
HXB2 Location Env
Author Location gp120 (HIV2ROD)
Epitope `HYQ(core)`
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* HIV-2 ROD
Species (Isotype) mouse
Ab Type C3
References Matsushita *et al.* 1995

- B2C: Viral neutralization was type-specific for HIV-2 ROD. Matsushita *et al.* [1995]

No. 979
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
Ab Type C3
References Wang *et al.* 2002b

- Autologous NAbs were studied in 3 patients on HAART that rebounded – phylogenetic analysis of env (V1-V5) sequences indicated that rebound viruses had evolved from or preexisted in baseline populations – HIV-1 rebound viruses from all 3 patients were resistant to neutralization by autologous IgG, unlike the baseline viruses – mutations in the C3 region was responsible for conferring neutralization resistance against autologous antibody in 2 of 3 patients. Wang *et al.* [2002b]

No. 980
MAb ID 1024
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
Ab Type C4
References Berman *et al.* 1997

- 1024: Binds to 1/7 isolates from breakthrough cases from a MN gp120 vaccine trial. Berman *et al.* [1997]

No. 981
MAb ID 4KG5
HXB2 Location Env
Author Location gp120 (JR-FL)
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
Ab Type C4, V3, V1-V2
References Zwick *et al.* 2003
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, structure, variant cross-recognition or cross-neutralization

- 4KG5: 4KG5, a single-chain Fv (scFv), reacts with a conformational epitope that is formed by the V1, V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. 4KG5 was derived from the serum of HIV-1 infected patient FDA2, who showed broad neutralizng activity, but is not itself neutralizing. Denaturation of gp120 abolished binding of 4KG5 and Fab b12. Addtionally, binding of 4KG5 was abrogated when any of the V1, V2 or V3 loops were deleted. Of a panel of Abs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions

diminished or abrogated binding: V2 loop MAbs (G3-4, G3-136), V3 loop MAbs (19b, 447-52D, hNM01, AH48, loop2, F425 B4e8, 694-88D), V3-C4 (G3-299, G3-42, G3-519, G3-537), CD4BS (b6, b3, F91, F105, 15e, L33, 1008-D, 654-30D, 559-64D, 1027-30D, Ia3, Ia7, FG39, Fbb14). MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1, V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. 4KG5 recognized HIV-1 envelope proteins derived from JR-FL, JR-CSF, BaL, ADA and R2, but not MN, DH123, HxB2, YU2, SF2 and 89.6. Binding of 4KG5 to different strains of HIV-1 env is probably due to sequence differences in V3 and C4, rather than V1 or V2. Zwick *et al.* [2003] (**antibody binding site definition and exposure**, **antibody generation**, **antibody interactions**, **variant cross-recognition or cross-neutralization**, **structure**)

No. 982
MAb ID 23A (2.3A)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen
Species (Isotype)
Ab Type C5
Research Contact James Robinson, Tulane University, LA
References Schulke *et al.* 2002; Binley *et al.* 1999; Fouts *et al.* 1997; Trkola *et al.* 1996a; Wu *et al.* 1996; Thali *et al.* 1993; Thali *et al.* 1992a

- 23A: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140. Schulke *et al.* [2002]
- 23A: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999]
- 23A: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – 23A bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997]
- 23A: C5 binding MAb – does not inhibit gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]
- 23A: Called 2.3A – Did not block ability of gp120-sCD4 complexes to inhibit MIP-1alpha binding – binds to gp41-binding domain of gp120. Wu *et al.* [1996]

No. 983
MAb ID D7324
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
HIV component: gp120
Species (Isotype) sheep
Ab Type C5
Research Contact Aalto BioReagents Ltd, Dublin, Ireland or Cliniqa Inc., Fallbrook, CA, USA
References Jeffs *et al.* 2004; Zwick *et al.* 2003; Herrera *et al.* 2003; Poignard *et al.* 2003; Basmaciogullari *et al.* 2002; Xiang *et al.* 2002a; Gram *et al.* 2002; Sanders *et al.* 2002; Binley *et al.* 1998; Mondor *et al.* 1998; Ugolini *et al.* 1997; Ditzel *et al.* 1997; Trkola *et al.* 1996a; Wyatt *et al.* 1995; Moore *et al.* 1993b; Moore *et al.* 1993a; Sattentau & Moore 1991; Moore 1990
Keywords antibody interactions, inter-clade comparisons, vaccine antigen design

- D7324: A set of oligomeric envelope proteins were made from six primary isolates for potenial use as vaccine antigens: 92/UG/037 (clade A), HAN2/2 (clade B), 92/BR25/025 (clade C), 92/UG/021 (clade D), 93/BR/029 (clade F) and MVP5180 (clade O). This was one of a panel of MAbs used to explore folding and exposure of well characterized epitopes. The clade C isolate BR25 is apparently misfolded, as conformation-dependent antibodies did not bind to it. D7324 bound to clade A, B, C, D and F HIV-1 primary isolates, but not to the group O protein. Polyclonal sera raised in rabbits against these antigens cross-bound the other antigens, but none of the sera had neutralizing activity. Jeffs *et al.* [2004] (**vaccine antigen design**, **inter-clade comparisons**)
- D7324: Used to capture gp120 onto solid phase for epitope mapping. Basmaciogullari *et al.* [2002]; Binley *et al.* [1998]; Ditzel *et al.* [1997]; Herrera *et al.* [2003]; Moore *et al.* [1993a,b]; Poignard *et al.* [2003]; Sanders *et al.* [2002]; Xiang *et al.* [2002a]
- D7324: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding polyclonal Ab that had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)

- D7324: Called NEA9205 – gp120 capture ELISAs with MAbs D7324 (anti-C-term) or 9205 (anti-V3) were compared in a study of orientation of glycosylation sites – CD4 binding could only inhibit deglycosylation when gp120 was bound to the plate by D7324, not by 9205, while Abs from HIV-1 infected people inhibited deglycosylation most effectively when gp120 was caught by 9205. Gram *et al.* [2002]
- D7324: Epitope in C5 – Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]
- D7324: Binds to the last 15 amino acids in gp120 – used for antigen capture ELISA. Wyatt *et al.* [1995]
- D7324: Binding unaltered by gp120 binding to sCD4, in contrast to 110.5, 9284, 50-69 and 98-6. Sattentau & Moore [1991]

No. 984
MAb ID 10/46c
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp120
Species (Isotype) rat
Ab Type CD4BS
References Peet *et al.* 1998; Jeffs *et al.* 1996; Cordell *et al.* 1991

- 10/46c: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 10/46c was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]
- 10/46c: Increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. Jeffs *et al.* [1996]

No. 985
MAb ID 1008-D
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Zwick *et al.* 2003; Zolla-Pazner *et al.* 1995
Keywords antibody interactions

- scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)

No. 986
MAb ID 1027-30-D (1027-30D)
HXB2 Location Env
Author Location Env
Epitope
Neutralizing
Immunogen
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny & Zolla-Pazner 2004; Zwick *et al.* 2003; Hioe *et al.* 2000
Keywords antibody interactions, review

- 1027-30D: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 1027-30-D: Called 1027-30D. scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- 1027-30-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. Hioe *et al.* [2000]

No. 987
MAb ID 1125H (1125h)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (MN)
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact Shermaine Tilley, Public Health Research Institute, USA

References Yang *et al.* 1998; Alsmadi & Tilley 1998; Wyatt *et al.* 1998; Pincus *et al.* 1996; Warrier *et al.* 1996; D'Souza *et al.* 1995; Pinter *et al.* 1993b; Wyatt *et al.* 1992; Thali *et al.* 1992a; Tilley *et al.* 1991a; Tilley *et al.* 1991b

- 1125H: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains. Alsmadi & Tilley [1998]
- 1125H: Called 1125h – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. Wyatt *et al.* [1998]
- 1125H: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. Yang *et al.* [1998]
- 1125H: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. Pincus *et al.* [1996]
- 1125H: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. Warrier *et al.* [1996]
- 1125H: Neutralization was MN specific – failed to neutralize JRCSF, and 2 B subtype and 1 D subtype primary isolates in a multi-laboratory study involving 11 labs. D'Souza *et al.* [1995]
- 1125H: Binding to soluble gp120 enhanced by the presence of an anti-V3 HuMAb, 41148D. Pinter *et al.* [1993b]
- 1125H: Amino acid substitutions in HXB2 that strongly inhibit binding: 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470, 480. Thali *et al.* [1992a]
- 1125H: Precipitation of Delta 297-329 env glycoprotein, with has a deleted V3 loop, is much more efficient that precipitation of wild type. Wyatt *et al.* [1992]
- 1125H: Binding to gp120 inhibited by CD4 – epitope is destroyed by reduction, but not by removal of N-linked sugars – potent neutralization of MN, RF, SF-2 and IIIB – neutralization synergy with anti-V3 MAb 4117C. Tilley *et al.* [1991a]

No. 988
MAb ID 1125H (1125h)
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing L (MN)
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact Shermaine Tilley, Public Health Research Institute, USA
References Pinter *et al.* 2004; Gorny & Zolla-Pazner 2004; Yang *et al.* 1998; Alsmadi & Tilley 1998; Wyatt *et al.* 1998; Pincus *et al.* 1996; Warrier *et al.* 1996; D'Souza *et al.* 1995; Pinter *et al.* 1993b; Wyatt *et al.* 1992; Thali *et al.* 1992a; Tilley *et al.* 1991a; Tilley *et al.* 1991b

Keywords ADCC, antibody binding site definition and exposure, antibody interactions, assay development, immunotoxin, inter-clade comparisons, review, structure, variant cross-recognition or cross-neutralization

- 1125H: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 1125H: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. Three anti-CD4BS MAbs were tested, including IgG1b12 which neutralizes both JRFL and SF162. The affinities for IgG1b12 and 5145A were similar for both JRFL and SF612, but 1125A bound with 2.5 fold higher affinity to SF162. 5145A and 1125H both preferentially neutralize SF162, but not JRFL, and the CD4BS is more sensitive to neutralization in the context of the SF162 V1V2 loop. This was also true for neutralization by sCD4. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 1125H: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains. Alsmadi & Tilley [1998] (**ADCC**)
- 1125H: Called 1125h – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. Wyatt *et al.* [1998] (**structure**)
- 1125H: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. Yang *et al.* [1998] (**assay development**)
- 1125H: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. Pincus *et al.* [1996] (**immunotoxin**)
- 1125H: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. Warrier *et al.* [1996] (**antibody interactions**)
- 1125H: Neutralization was MN specific – failed to neutralize JRCSF, and 2 B subtype and 1 D subtype primary isolates in a multi-laboratory study involving 11 labs. D'Souza *et al.* [1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 1125H: Binding to soluble gp120 enhanced by the presence of an anti-V3 HuMAb, 41148D. Pinter *et al.* [1993b] (**antibody interactions**)
- 1125H: Amino acid substitutions in HXB2 that strongly inhibit binding: 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470,

B Cell

480. Thali *et al.* [1992a] (**antibody binding site definition and exposure**)
- 1125H: Precipitation of Delta 297-329 env glycoprotein, with has a deleted V3 loop, is much more efficient that precipitation of wild type. Wyatt *et al.* [1992] (**antibody binding site definition and exposure**)
- 1125H: Binding to gp120 inhibited by CD4 – epitope is destroyed by reduction, but not by removal of N-linked sugars – neutralization of MN, RF, SF-2 and IIIB – neutralization synergy with anti-V3 MAb 4117C. Tilley *et al.* [1991a] (**antibody binding site definition and exposure**, **antibody interactions**, **variant cross-recognition or cross-neutralization**)

No. 989
MAb ID 120-1B1
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen L
Species (Isotype) human
Ab Type CD4BS
Research Contact Virus Testing Systems Corp., Houston, TX
References Gorny & Zolla-Pazner 2004; Watkins *et al.* 1993
Keywords antibody binding site definition and exposure, review

- 120-1B1: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 120-1B1: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – 120-1B1 was not affected by this mutation. Watkins *et al.* [1993] (**antibody binding site definition and exposure**)

No. 990
MAb ID 1202-D (1202-30-D)
HXB2 Location Env
Author Location Env
Epitope
Neutralizing
Immunogen
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Hioe *et al.* 2000; Nyambi *et al.* 1998
Keywords inter-clade comparisons, review

- 1202-D: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 1202-D: Called 1202-30D – Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. Hioe *et al.* [2000]
- 1202-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 1202-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 1202-D did not bind to any B clade viruses, and weakly bound A, C, and G clade isolates – 559/64-D, 558-D and 1202-D had similar reactivities. Nyambi *et al.* [1998] (**inter-clade comparisons**)

No. 991
MAb ID 1331E
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny & Zolla-Pazner 2004; Gorny *et al.* 2000
Keywords antibody binding site definition and exposure, review

- 1331E: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 1331E: Inhibits sCD4 binding to rec gp120 LAI – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)

No. 992
MAb ID 1570 (1570A, 1570C, 1570D)
HXB2 Location Env
Author Location Env (PR12, BH10)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS

References Gorny & Zolla-Pazner 2004; Jeffs *et al.* 2001
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 1570: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 1570: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – three MAbs were isolated from one individual, 1570A, C and D but all were determined to have the same V(H)3 region – 1570 was able to bind to a panel of recombinant proteins from the A, B, C, D, and E subtypes. Jeffs *et al.* [2001] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 993
MAb ID 1595
HXB2 Location Env
Author Location Env (PR12, BH10)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Jeffs *et al.* 2001
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 1595: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 1595: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – 1595 was able to bind gp120 from the A, B, and D clades from a panel of recombinant proteins from the A, B, C, D, and E subtypes. Jeffs *et al.* [2001] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 994
MAb ID 1599
HXB2 Location Env
Author Location Env (PR12, BH10)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Jeffs *et al.* 2001
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 1599: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 1599: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – 1599 was able to bind gp120 only from the B clade from a panel of recombinant proteins from the A, B, C, D, and E subtypes. Jeffs *et al.* [2001] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 995
MAb ID 15e (1.5e, 1.5E, 15E)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact James Robinson, Tulane University, LA, and David Ho, ADARC, NY, NY
References Nabatov *et al.* 2004; Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Raja *et al.* 2003; Pantophlet *et al.* 2003a; Kwong *et al.* 2002; Zhang *et al.* 2002; Xiang *et al.* 2002b; Kolchinsky *et al.* 2001; Park *et al.* 2000; Sullivan *et al.* 1998a; Fouts *et al.* 1998; Trkola *et al.* 1998; Binley *et al.* 1998; Sullivan *et al.* 1998b; Parren *et al.* 1998a; Wyatt *et al.* 1998; Parren *et al.* 1997b; Berman *et al.* 1997; Wyatt *et al.* 1997; Li *et al.* 1997; Fouts *et al.* 1997; Binley *et al.* 1997a; Wisnewski *et al.* 1996; McDougal *et al.* 1996; Trkola *et al.* 1996a; Poignard *et al.* 1996a; Moore & Sodroski 1996; McKeating *et al.* 1996; Lee *et al.* 1995; Sattentau & Moore 1995; Moore *et al.* 1994a; Moore *et al.* 1994b; Cook *et al.* 1994; Thali *et al.* 1994; Bagley *et al.* 1994; Wyatt *et al.* 1993; Watkins *et al.* 1993; Thali *et al.* 1993; Moore & Ho 1993; Takeda *et al.* 1992; Thali *et al.* 1992a; Wyatt *et al.* 1992; Ho *et al.* 1992; Koup *et al.* 1991; Ho *et al.* 1991b; Cordell *et al.* 1991; Thali *et al.* 1991; Robinson *et al.* 1990a
Keywords ADCC, adjuvant comparison, antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, brain/CSF, co-receptor, enhancing activity, inter-clade comparisons, review, struc-

ture, vaccine antigen design, variant cross-recognition or cross-neutralization

- 15e: UK Medical Research Council AIDS reagent: ARP3016.
- 15e: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 15e: A set of HIV-1 chimeras that altered V3 net charge and glycosylation patterns in V1V2 and V3, involving inserting V1V2 loops from a late stage primary isolate taken after the R5 to X4 switch, were studied with regard to phenotype, co-receptor usage, and MAb neutralization. The loops were cloned into a HXB2 envelope with a LAI viral backbone. It was observed that the addition of the late-stage isolate V1V2 region and the loss of V3-linked glycosylation site in the context of high positive charge gave an X4 phenotype. R5X4, R5, and X4 viruses were generated, and sCD4, 2G12 and b12 neutralization resistance patterns were modified by addition of the late stage V1V2, glycosylation changes, and charge in concert, while neutralization by 2F5 was unaffected. 15e, 17b, and 48d could not neutralize any of the variants tested. Nabatov *et al.* [2004] (**antibody binding site definition and exposure**, **co-receptor**)
- 15e: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished. Pantophlet *et al.* [2003a] (**antibody binding site definition and exposure**)
- 15e: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- 15e: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs F105, 15e, and IgG1b12 as well as their Fab fragments inhibited CD4-independent binding of the V1/V2 loop-deleted gp120 glycoproteins of R5 HIV-1 isolates ADA, YU2 and JRFL and to CCR5 in a concentration dependent manner. Raja *et al.* [2003] (**co-receptor**)
- 15e: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- 15e: Called 1.5e. Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol, The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- 15e: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b] (**antibody binding site definition and exposure**)
- 15e: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002] (**antibody binding site definition and exposure**)
- 15e: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 15e. Kolchinsky *et al.* [2001] (**antibody binding site definition and exposure**)
- 15e: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-

100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000] (**antibody binding site definition and exposure**)

- 15e: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type. Binley *et al.* [1998] (**antibody binding site definition and exposure**)
- 15e: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer. Fouts *et al.* [1998] (**antibody binding site definition and exposure**)
- 15e: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**antibody binding site definition and exposure**)
- 15e: Competes with CG-10 binding, a MAb raised against a gp120 CD4 complex, this was probably due to the disruption of CD4-gp120 by 15e. Sullivan *et al.* [1998b] (**antibody binding site definition and exposure**, **antibody interactions**)
- 15e: Called 1.5e – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – 1.5e enhances and does not neutralize YU2 env even at 50 ug/ml. Sullivan *et al.* [1998a] (**antibody binding site definition and exposure**)
- 15e: No detectable neutralizing activity among primary isolates with different co-receptor usage – some neutralization of TCLA strains. Trkola *et al.* [1998] (**variant cross-recognition or cross-neutralization**)
- 15e: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. Wyatt *et al.* [1998] (**structure**)
- 15e: Called 1.5E – Binds to 7/7 isolates from breakthrough cases from a MN gp120 vaccine trial. Berman *et al.* [1997] (**variant cross-recognition or cross-neutralization**)
- 15e: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 15e bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- 15e: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 15e could only achieve 50% neutralization, but could act synergistically with anti-V3 MAb 694/98-D to achieve 90% Li *et al.* [1997] (**antibody interactions**)
- 15e: Neutralizes TCLA strains, but not primary isolates. Parren *et al.* [1997b]
- 15e: Does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-93, are deleted. Wyatt *et al.* [1997] (**antibody binding site definition and exposure**)
- 15e: Neutralizes HIV-1 LAI less potently than V3 specific MAbs. McDougal *et al.* [1996]
- 15e: Called 1.5e – Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. McKeating *et al.* [1996] (**variant cross-recognition or cross-neutralization**)
- 15e: gp120 binding enhanced by anti-V3 MAb 5G11 and anti-V2 MAb G3-136 – binding inhibited by other CD4 binding site MAbs, antibodies that bind to gp120 only when CD4 is bound, and CD4-IgG. Moore & Sodroski [1996] (**antibody interactions**)
- 15e: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50-69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs. Poignard *et al.* [1996a] (**antibody interactions**)
- 15e: Inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a] (**antibody binding site definition and exposure**)
- 15e: 15e is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- 15e: The V4 and V5 domains are essential for 1.5e binding, in contrast to the V1, V2, and V3 loops. Lee *et al.* [1995] (**antibody binding site definition and exposure**)
- 15e: Binds with higher affinity to monomer than to oligomer, moderate association rate. Sattentau & Moore [1995] (**antibody binding site definition and exposure**)
- 15e: Heavy chain is V HIV, V2-1 – light chain is V_kappaI, Hum01/012. Compared to 21h and F105. Bagley *et al.* [1994] (**antibody sequence, variable domain**)
- 15e: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – anti-CD4 MAbs moderately inhibit gp120 binding to GalCer, possibly through steric hindrance – binding of GalCer to gp120 inhibited but did not completely block 15e binding. Cook *et al.* [1994] (**antibody binding site definition and exposure**, **brain/CSF**)
- 15e: Cross-reactive with gp120 proteins from clades B and D, less so with A and C, and not reactive with clade E and F. Moore *et al.* [1994b] (**inter-clade comparisons**)
- 15e: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 21h and 17b) Thali *et al.* [1994] (**antibody binding site definition and exposure**)
- 15e: Conformational, does not bind denatured gp120 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120. Moore & Ho [1993] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 15e: Called 15E – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – 15E neutralization was not affected by this mutation. Watkins *et al.* [1993] (**antibody binding site definition and exposure**)

- 15e: Binding to Delta V1/2 and Delta V1/2/3 mutant glycoproteins is greater than binding to wildtype gp120. Wyatt *et al.* [1993] (**antibody binding site definition and exposure**)
- 15e: gp120 mutants that affect 15e epitope binding: 113, 257, 368, 370, 421, 427, 475 – four of these coincide with amino acids important for the CD4 binding domain. Ho *et al.* [1992] (**antibody binding site definition and exposure**)
- 15e: Amino acid substitutions in HXB2 that strongly inhibit binding, similar to Ho *et al.* [1992], some additional, 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470, 480 Thali *et al.* [1992a]. Ho *et al.* [1992]; Thali *et al.* [1992a] (**antibody binding site definition and exposure**)
- 15e: Called N70-1.5e – does not enhance infection of HIV-1 IIIB and MN. Thali *et al.* [1992a] (**enhancing activity**)
- 15e: Precipitation of Delta 297-329 env glycoprotein, with a deleted V3 loop, is much more efficient that precipitation of wild type. Wyatt *et al.* [1992] (**antibody binding site definition and exposure**)
- 15e: Cross-competes with MAbs ICR 39.13g and ICR 39.3b. Cordell *et al.* [1991] (**antibody interactions**)
- 15e: Broadly neutralizing, binds multiple strains, competes with CD4 for gp120 binding, DTT reduction of env abrogates binding – more potent blocking of gp120-sCD4 binding than MAbs G3-536 and G3-537. Ho *et al.* [1991b] (**adjuvant comparison**, **variant cross-recognition or cross-neutralization**)
- 15e: Binds to gp120 of HIV-1 IIIB, but not RF – mediates ADCC – deletion of the V3 loop from gp120 does not alter ADCC activity. Koup *et al.* [1991] (**ADCC**, **variant cross-recognition or cross-neutralization**)

No. 996
MAb ID 21h (2.1H)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type CD4BS
Research Contact James Robinson, Tulane University, LA
References Gorny & Zolla-Pazner 2004; Xiang *et al.* 2002b; Fouts *et al.* 1998; Parren *et al.* 1998a; Wyatt *et al.* 1998; Parren *et al.* 1997b; Wyatt *et al.* 1997; Ugolini *et al.* 1997; Li *et al.* 1997; Fouts *et al.* 1997; Binley *et al.* 1997a; McKeating *et al.* 1996; Wisnewski *et al.* 1996; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; Thali *et al.* 1994; Bagley *et al.* 1994; Moore *et al.* 1994a; Moore *et al.* 1994b; Moore & Ho 1993; Wyatt *et al.* 1993; Ho *et al.* 1992; Thali *et al.* 1992a; Ho *et al.* 1991b
Keywords acute infection, antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, binding affinity, inter-clade comparisons, review, structure, variant cross-recognition or cross-neutralization

- 21h: UK Medical Research Council AIDS reagent: ARP3017.
- 21h: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 21h: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations—375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91) was markedly reduced—IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced—2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope—another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b] (**antibody binding site definition and exposure**)
- 21h: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer – conclusions of this paper contrast with Parren *et al.* [1998a] Fouts *et al.* [1998]. Fouts *et al.* [1998]; Parren *et al.* [1998a] (**binding affinity**)
- 21h: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**antibody binding site definition and exposure**)
- 21h: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. Wyatt *et al.* [1998] (**antibody binding site definition and exposure**, **structure**)
- 21h: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 21h bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- 21h: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 67 mug/ml. Li *et al.* [1997] (**variant cross-recognition or cross-neutralization**)
- 21h: Neutralizes TCLA strains, but not primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 21h: Viral binding inhibition by 21h strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997] (**antibody binding site definition and exposure**)
- 21h: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding – major deletions in C1 and C5 and deletions of the V1V2 and V3 loops do not diminish binding. Wyatt *et al.* [1997] (**antibody binding site definition and exposure**)
- 21h: Called 2.1H – Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. McKeating *et al.* [1996] (**variant cross-recognition or cross-neutralization**)

- 21h: Anti-CD4 binding site MAb – reciprocal inhibition by anti-C1, -C4 and other anti-CD4 binding site antibodies – enhanced by some anti-V2 MAbs and anti-V3 MAb 5G11 – enhances binding of some anti-V3 and -V2 MAbs. Moore & Sodroski [1996] (**antibody interactions**)
- 21h: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50-69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs. Poignard *et al.* [1996a] (**antibody binding site definition and exposure**, **antibody interactions**)
- 21h: 21h is V H3 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- 21h: Binds with higher affinity to monomer than to oligomer, moderate association rate. Sattentau & Moore [1995] (**antibody binding site definition and exposure**)
- 21h: Heavy chain is V HIII, VDP-35 – light chain is V_lambdaIIIa, Hum318. Compared to 15e and F105. Bagley *et al.* [1994] (**antibody sequence, variable domain**)
- 21h: Has strong cross-reactivity with gp120 monomers from most subtypes, A-F, with the least reactivity to clade E. Moore *et al.* [1994b] (**inter-clade comparisons**)
- 21h: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies. Moore *et al.* [1994a] (**acute infection**)
- 21h: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 15e and 17b) Thali *et al.* [1994] (**variant cross-recognition or cross-neutralization**)
- 21h: Conformational, does not bind denatured gp120 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120. Moore & Ho [1993] (**antibody binding site definition and exposure**)
- 21h: Binding to Delta V1/2 and Delta V1/2/3 mutant glycoproteins is greater than binding to wildtype gp120. Wyatt *et al.* [1993] (**antibody binding site definition and exposure**)
- 21h: Amino acid substitutions in HXB2 that inhibit binding, some shared with CD4 binding inhibition, 88, 113, 257, 368, 370, 421, 470, 480. Thali *et al.* [1992a] (**antibody binding site definition and exposure**)

No. 997
MAb ID 28A11/B1
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type CD4BS
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 28A11/B1: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 28A11/B1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—28A11/B1 was one of these four MAbs. He *et al.* [2002] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 998
MAb ID 2G6
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
Ab Type CD4BS
Research Contact Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, or Polymun Scientific Inc., Vienna, Austria
References Gorny & Zolla-Pazner 2004; Parren *et al.* 1998a; Fouts *et al.* 1998
Keywords antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization

- 2G6: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 2G6: Binds to JRFL oligomer with an affinity comparable to IgG1b12, but does not neutralize the virus, so binding of oligomer is not always predictive of neutralization – conclusions of this paper contrast with Parren *et al.* [1998a] – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect Fouts *et al.* [1998]. Fouts *et al.* [1998]; Parren *et al.* [1998a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

No. 999
MAb ID 35F3/E2
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing L
Immunogen Vaccine

Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type CD4BS
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 35F3/E2: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 35F3/E2: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—35F3/E2 was one of these four MAbs. He *et al.* [2002] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 1000
MAb ID 38G3/A9
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type CD4BS
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords variant cross-recognition or cross-neutralization

- 38G3/A9: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**)
- 38G3/A9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—38G3/A9 was one of these four MAbs. He *et al.* [2002] (**variant cross-recognition or cross-neutralization**)

No. 1001
MAb ID 428
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Jeffs *et al.* 1996; Karwowska *et al.* 1992a

- 428: Slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. Jeffs *et al.* [1996]

No. 1002
MAb ID 448-D (448D)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Wyatt *et al.* 1998; Li *et al.* 1997; Manca *et al.* 1995a; Forthal *et al.* 1995; Laal *et al.* 1994; Spear *et al.* 1993; McKeating *et al.* 1992c; Karwowska *et al.* 1992a
Keywords ADCC, antibody binding site definition and exposure, antibody interactions, complement, enhancing activity, inter-clade comparisons, review, structure, variant cross-recognition or cross-neutralization

- 448-D: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 448-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12. Nyambi *et al.* [2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 448-D: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. Wyatt *et al.* [1998] (**structure**)
- 448-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env. Li *et al.* [1997] (**variant cross-recognition or cross-neutralization**)
- 448-D: Neutralizing activity, positive ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995] (**ADCC**, **enhancing activity**)
- 448-D: Virions complexed to gp120 Ab facilitate presentation of p66 RT epitopes to Th cells. Manca *et al.* [1995a]

- 448-D: Dissociation constant gp120 IIIB 0.029 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D. Laal *et al.* [1994] (**antibody interactions**)
- 448-D: Did not mediate deposition of complement component C3 on HIV infected cells. Spear *et al.* [1993] (**complement**)
- 448-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay. Karwowska *et al.* [1992a] (**antibody binding site definition and exposure**)
- 448-D: Called 448D – blocks gp120-CD4 binding – substitutions at gp120 residues 88, 113, 117, 257, 368 and 370 reduce binding – epitope similar to rat MAbs 39.13g and 39.3b. McKeating *et al.* [1992c] (**antibody binding site definition and exposure**)

No. 1003
MAb ID 46D2/D5
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type CD4BS
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He *et al.* 2002

- 44D2/D5: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—44D2/D5 could not neutralize autologous SF162, and while it was cross-reactive, it was at lower affinity. He *et al.* [2002]

No. 1004
MAb ID 48-16
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgGκ)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Fevrier *et al.* 1995
Keywords antibody binding site definition and exposure, binding affinity, review, variant cross-recognition or cross-neutralization

- 48-16: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database. Most neutralize TCLA strains only, 48-16 is one of four that are non-neutralizing. Gorny & Zolla-Pazner [2004] (**review**)
- 48-16: Broadly cross-reactive, reacts outside the CD4 binding site and V3 region—competes with sera from 45 seropositive subjects—binding affinity 2–5 $\times 10^{-9}$ M. Fevrier *et al.* [1995] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **binding affinity**)

No. 1005
MAb ID 50-61A
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgGκ)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Fevrier *et al.* 1995
Keywords binding affinity, review, variant cross-recognition or cross-neutralization

- 50-61A: Neutralizes lab strains LAI and SF2 – competes with sera from 45 seropositive subjects – binding affinity 2.4 x 10^{-10} M. (**variant cross-recognition or cross-neutralization**, **binding affinity**)
- 50-61A: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)

No. 1006
MAb ID 5145A
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type CD4BS
Research Contact Abraham Pinter, Public Health Research Institute, Newark, NJ, 07103. pinter@phri.org.
References Pinter *et al.* 2004; Gorny & Zolla-Pazner 2004; He *et al.* 2002; Alsmadi & Tilley 1998; Pincus *et al.* 1996; Warrier *et al.* 1996; Pinter *et al.* 1993a
Keywords ADCC, antibody interactions, immunotoxin, variant cross-recognition or cross-neutralization

- 5145A: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**)
- 5145A: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. Three

anti-CD4BS MAbs were tested, including IgG1b12, which neutralizes both JRFL and SF162. The affinities for IgG1b12 and 5145A were similar for both JRFL and SF612, but 1125A bound with 2.5 fold higher affinity to SF162. 5145A and 1125H both preferentially neutralize SF162, but not JRFL, and the CD4BS is more sensitive to neutralization in the context of the SF162 V1V2 loop. This was also true for neutralization by sCD4. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)

- 5145A: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A, 4117C and 697D were used as controls. He *et al.* [2002]
- 5145A: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains. Alsmadi & Tilley [1998] (**ADCC**)
- 5145A: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. Pincus *et al.* [1996] (**immunotoxin**)
- 5145A: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. Warrier *et al.* [1996] (**antibody interactions**)
- 5145A: Potent and broadly cross-reactive neutralization of lab strains. Pinter *et al.* [1993a] (**variant cross-recognition or cross-neutralization**)

No. 1007
MAb ID 558-D
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny & Zolla-Pazner 2004; Nyambi *et al.* 1998; McKeating *et al.* 1992c
Keywords antibody binding site definition and exposure, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 558-D: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 558-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 558-D did not bind to any B clade viruses, and weakly bound to clade A, C, and G isolates – 559/64-D, 558-D and 1202-D had similar reactivities. Nyambi *et al.* [1998] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 558-D: Blocks gp120-CD4 binding – binds a panel of mutants all except for 256 S/Y and 262 N/T, which are probably conformationally disruptive. McKeating *et al.* [1992c] (**antibody binding site definition and exposure**)

No. 1008
MAb ID 559/64-D (559, 559-64D)
HXB2 Location Env
Author Location gp120 (LAI)
Epitope
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny & Zolla-Pazner 2004; Zwick *et al.* 2003; York *et al.* 2001; Hioe *et al.* 2001; Nyambi *et al.* 2000; Hioe *et al.* 2000; Gorny *et al.* 2000; Nyambi *et al.* 1998; Hioe *et al.* 1997b; Hioe *et al.* 1997a; Jeffs *et al.* 1996; Forthal *et al.* 1995; Stamatatos & Cheng-Mayer 1995; Spear *et al.* 1993; McKeating *et al.* 1992c; Karwowska *et al.* 1992a
Keywords ADCC, antibody binding site definition and exposure, antibody interactions, assay development, complement, enhancing activity, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 559/64D: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 559/64D: called 559-64D: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- 559/64-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFNγ production—anti-CD4BS MAbs inhibit gp120 presentation by altering the uptake and/or processing of gp120 by the APCs, not by blocking of gp120 attachment to CD4 on the surface of APCs. Hioe *et al.* [2001]
- 559/64-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4 induced or CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change

in TCLA lines that make them more susceptible to NAbs alters some step after binding. York *et al.* [2001] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

- 559/64-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer. Gorny *et al.* [2000] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 559/64-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. Hioe *et al.* [2000]
- 559/64-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 559/64-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 559/64-D did not bind to any B clade viruses, and weakly bound clade A, C, and G isolates – 559/64-D, 558-D and 1202-D had similar reactivities. Nyambi *et al.* [1998] (**antibody binding site definition and exposure**, **inter-clade comparisons**)
- 559/64-D: Used in the development of resting cell neutralization assay. Hioe *et al.* [1997a] (**assay development**)
- 559/64-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 559/64-D: Called 559 – slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. Jeffs *et al.* [1996] (**antibody binding site definition and exposure**)
- 559/64-D: Neutralizing activity, no ADCC activity, and no viral enhancing activity. Forthal *et al.* [1995] (**ADCC**, **enhancing activity**, **variant cross-recognition or cross-neutralization**)
- 559/64-D: Called 559-64D – The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – CD4BS loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a and to T-cell tropic SF2 – binding of anti-CD4BS MAbs to SF2 resulted in a significant amount of dissociation of gp120 from virion surface. Stamatatos & Cheng-Mayer [1995] (**antibody binding site definition and exposure**)
- 559/64-D: Did not mediate deposition of complement component C3 on HIV infected cells. Spear *et al.* [1993] (**complement**)
- 559/64-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay. Karwowska *et al.* [1992a] (**antibody binding site definition and exposure**)

No. 1009
MAb ID 55D5/F9
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type CD4BS
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords review, variant cross-recognition or cross-neutralization

- 55D5/F9: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database. Most neutralize TCLA strains only, this is one of four that are non-neutralizing. Gorny & Zolla-Pazner [2004] (**review**)
- 55D5/F9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—55D5/F9 was one of these four MAbs. He *et al.* [2002] (**variant cross-recognition or cross-neutralization**)

No. 1010
MAb ID 588-D (588)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS

Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY

References Nyambi *et al.* 2000; Hioe *et al.* 2000; Nyambi *et al.* 1998; Jeffs *et al.* 1996; Moore & Ho 1993; Buchbinder *et al.* 1992; Karwowska *et al.* 1992a

- 588-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. Hioe *et al.* [2000]
- 588-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12. Nyambi *et al.* [2000]
- 588-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 588-D did not bind to any B clade viruses, and weakly bound a clade A, C, and G clade isolate – 559/64-D, 558-D and 1202-D reacted had similar reactivities. Nyambi *et al.* [1998]
- 588-D: Called 588 – slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. Jeffs *et al.* [1996]
- 588-D: Weak neutralization of IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120. Moore & Ho [1993]
- 588-D: 4-fold increase in neutralization potency for 588-D when combined 1:1 with human MAb 447-D. Buchbinder *et al.* [1992]
- 588-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay. Karwowska *et al.* [1992a]

No. 1011
MAb ID 654-D (654-30D, 654/30D, 654-D100, 654.30D, 654)
HXB2 Location Env
Author Location gp120 (LAI)
Epitope
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgGκ)
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY

References Gorny & Zolla-Pazner 2004; Zwick *et al.* 2003; Gorny *et al.* 2002; Verrier *et al.* 2001; Nyambi *et al.* 2000; Hioe *et al.* 2001; Hioe *et al.* 2000; Gorny *et al.* 2000; Hioe *et al.* 1999; Stamatatos & Cheng-Mayer 1998; Nyambi *et al.* 1998; Schonning *et al.* 1998; Gorny *et al.* 1998; Hioe *et al.* 1997b; Gorny *et al.* 1997; Stamatatos *et al.* 1997; Li *et al.* 1997; Stamatatos & Cheng-Mayer 1995; Gorny *et al.* 1994; Laal *et al.* 1994; Karwowska *et al.* 1993

Keywords antibody binding site definition and exposure, antibody interactions, binding affinity, enhancing activity, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization

- 654-D: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 654-D: Called 654-30D. scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- 654-D: Called 654: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions and the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), and MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) Gorny *et al.* [2002]
- 654-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFN gamma production – anti-CD4BS MAbs inhibit gp120 presentation by altering the uptake and/or processing of gp120 by the APCs, not by blocking of gp120 attachment to CD4 on the surface of APCs. Hioe *et al.* [2001]
- 654-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6—six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D, while six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281—no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 654-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer.

Gorny *et al.* [2000] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

- 654-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – MAb 654-D strongly diminished proliferation – there is a discrepancy in isotyping this antibody, previous reports indicated IgG1kappa, while Hioe suggests it is IgG1lambda. Hioe *et al.* [2000]
- 654-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12 – 654-D had the weakest binding among CD4BS MAbs, binding to only 4/26 isolates. Nyambi *et al.* [2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 654-D: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs. Hioe *et al.* [1999]
- 654-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind very weakly without clade specificity to virions, but bound well to soluble gp120 – 654-D bound only to JRFL. Nyambi *et al.* [1998] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 654-D: Called 654-D100 – 654-D100 and IgG1b12 neutralized viruses HIV-BRU and a mutated virus that lacks the V3 loop glycan equally effectively – in contrast, sera from guinea pigs immunized with BRU gp120 neutralize viruses more effectively that lack the V3 glycan. Schonning *et al.* [1998] (**variant cross-recognition or cross-neutralization**)
- 654-D: Called 654.30D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 slightly allowed neutralization by CD4BS MAb 654.30D. Stamatatos & Cheng-Mayer [1998] (**antibody binding site definition and exposure**, **inter-clade comparisons**)
- 654-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 654-D: Called 654-30D – One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env. Li *et al.* [1997] (**variant cross-recognition or cross-neutralization**)
- 654-D: Anti-CD4 BS MAb 654-30D and IgG1b12 have comparable binding affinities, neither mediates gp120-virion dissociation, but IgG1b12 can neutralize SF128A and SF162 and 654-D cannot – 654-D actually enhances infection by both viruses in primary macrophages. Stamatatos *et al.* [1997] (**enhancing activity**, **binding affinity**)
- 654-D: Called 654-30D – The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – CD4BS loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a and to T-cell tropic SF2 – binding of anti-CD4BS MAbs to SF2 resulted in a significant amount of dissociation of gp120 from virion surface. Stamatatos & Cheng-Mayer [1995] (**antibody binding site definition and exposure**)
- 654-D: Mild oxidation of carbohydrate moieties inhibits binding. Gorny *et al.* [1994] (**antibody binding site definition and exposure**)
- 654-D: Dissociation constant gp120 IIIB 0.008 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D – reported to be human(IgG1lambda) Laal *et al.* [1994] (**antibody interactions**, **kinetics**)

No. 1012
MAb ID 67G6/C4
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type CD4BS
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords review, variant cross-recognition or cross-neutralization

- 67G6/C4: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database. Most neutralize TCLA strains only, this MAb is one of four that are non-neutralizing. Gorny & Zolla-Pazner [2004] (**review**)
- 67G6/C4: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally

sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—67G6/C4 could not neutralize autologous SF162, and its binding was strain-specific. He *et al.* [2002] (**variant cross-recognition or cross-neutralization**)

No. 1013
MAb ID 729-D (729-30D)
HXB2 Location Env
Author Location gp120 (LAI)
Epitope
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny & Zolla-Pazner 2004; Gorny *et al.* 2000; Parren *et al.* 1997b; Li *et al.* 1997; D'Souza *et al.* 1997; Laal *et al.* 1994
Keywords antibody binding site definition and exposure, antibody interactions, kinetics, review, variant cross-recognition or cross-neutralization

- 729-D: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 729-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)
- 729-D: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – reported here to have a lambda light chain, but originally reported in Laal *et al.* [1994] to be IgG1kappa D'Souza *et al.* [1997]. D'Souza *et al.* [1997]; Laal *et al.* [1994] (**variant cross-recognition or cross-neutralization**)
- 729-D: Called 720-30D – one of 14 human MAbs tested for ability to neutralize chimeric SHIV-vpu+, which expressed HIV-1 IIIB env. Li *et al.* [1997] (**variant cross-recognition or cross-neutralization**)
- 729-D: Neutralizes TCLA strains, but not primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 729-D: Dissociation constant gp120 IIIB 0.025 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D. Laal *et al.* [1994] (**antibody interactions**, **kinetics**)

No. 1014
MAb ID 830D (830-D)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Hioe *et al.* 2000; Wyatt *et al.* 1998; Hioe *et al.* 1997b
Keywords review, structure, variant cross-recognition or cross-neutralization

- 830D: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- 830D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. Hioe *et al.* [2000]
- 830D: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. Wyatt *et al.* [1998] (**structure**)
- 830D: Called 830-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)

No. 1015
MAb ID 9CL
HXB2 Location Env
Author Location gp120 (LAI)
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny & Zolla-Pazner 2004; Gorny *et al.* 2000
Keywords antibody binding site definition and exposure, review

- 9CL: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)

- 9CL: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)

No. 1016
MAb ID BM12
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Kessler *et al.* 1995

- BM12: Broad cross-clade neutralization of primary isolates – additive effect in combination with MAb 2F5. Kessler *et al.* [1995]

No. 1017
MAb ID D20
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1997; Otteken *et al.* 1996; Richardson *et al.* 1996; Broder *et al.* 1994; Earl *et al.* 1994
Keywords antibody binding site definition and exposure, antibody generation

- D20: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D20 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. Sugiura *et al.* [1999] (**antibody binding site definition and exposure**)
- D20: Used for comparison in a study of gp41 antibodies – D20 binds to a greater extent to cell surface expressed Env than any of 38 conformation dependent anti-gp41 MAbs. Earl *et al.* [1997] (**antibody binding site definition and exposure**)
- D20: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp160 revealed that these anti-CD4 MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes. Otteken *et al.* [1996]
- D20: Human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4. Richardson *et al.* [1996]
- D20: Binding completely blocked by pooled human sera. Broder *et al.* [1994]
- D20: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994] (**antibody generation**)

No. 1018
MAb ID D21
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D21: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D21 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. Sugiura *et al.* [1999]
- D21: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1019
MAb ID D24
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D24: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D24 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. Sugiura *et al.* [1999]
- D24: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1020
MAb ID D25
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing

Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D25: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D25 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. Sugiura *et al.* [1999]
- D25: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1021
MAb ID D28
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D28: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D28 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. Sugiura *et al.* [1999]
- D28: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1022
MAb ID D35
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D35: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D35 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. Sugiura *et al.* [1999]
- D35: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1023
MAb ID D39
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D39: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D39 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. Sugiura *et al.* [1999]
- D39: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1024
MAb ID D42
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D42: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D42 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. Sugiura *et al.* [1999]
- D42: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1025
MAb ID D52

HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D52: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D52 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. Sugiura *et al.* [1999]
- D52: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1026
MAb ID D53
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D53: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D53 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. Sugiura *et al.* [1999]
- D53: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1027
MAb ID D60
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Richardson *et al.* 1996; Earl *et al.* 1994

- D60: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D60 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. Sugiura *et al.* [1999]
- D60: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1028
MAb ID DA48
HXB2 Location Env
Author Location gp120 (BRU)
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Sullivan *et al.* 1998a; Parren *et al.* 1998a
Keywords antibody binding site definition and exposure, antibody generation, binding affinity, review, variant cross-recognition or cross-neutralization

- DO8i: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- DA48: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**binding affinity**)
- DA48: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab Ab fragment DA48 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism – while DA48 enhances YU2, it neutralizes HXBc2 – DA48 was obtained by panning libraries derived from bone marrow from a >15 year long term non-progressor against BRU gp120. Sullivan *et al.* [1998a] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**)

No. 1029
MAb ID DO8i
HXB2 Location Env
Author Location gp120 (BRU)

Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Sullivan *et al.* 1998a; Parren *et al.* 1998a

- DO8i: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- DO8i – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment DO8i also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 – DO8i was obtained by panning libraries derived from bone marrow from a long term asymptomatic donor against BRU gp120. Sullivan *et al.* [1998a]

No. 1030
MAb ID F105 (F-105)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact Marshall Posner, Boston MA
References Ling *et al.* 2004; Biorn *et al.* 2004; Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Ohagen *et al.* 2003; Raja *et al.* 2003; Xiang *et al.* 2003; Poignard *et al.* 2003; Pantophlet *et al.* 2003a; Kwong *et al.* 2002; Cavacini *et al.* 2002; Ling *et al.* 2002; Liu *et al.* 2002; Ferrantelli & Ruprecht 2002; Zhang *et al.* 2002; Basmaciogullari *et al.* 2002; Grundner *et al.* 2002; Edwards *et al.* 2002; Xiang *et al.* 2002b; Chakrabarti *et al.* 2002; Xu *et al.* 2002; Yang *et al.* 2002; York *et al.* 2001; Kolchinsky *et al.* 2001; Si *et al.* 2001; Yang *et al.* 2000; Park *et al.* 2000; Fortin *et al.* 2000; Baba *et al.* 2000; Robert-Guroff 2000; Oscherwitz *et al.* 1999a; Cavacini *et al.* 1999; Giraud *et al.* 1999; Sugiura *et al.* 1999; Kropelin *et al.* 1998; Sullivan *et al.* 1998a; Brand *et al.* 1998; Cavacini *et al.* 1998a; Li *et al.* 1998; Cavacini *et al.* 1998b; Wyatt *et al.* 1998; Wyatt *et al.* 1997; Cao *et al.* 1997b; Li *et al.* 1997; D'Souza *et al.* 1997; Parren *et al.* 1997b; Chen *et al.* 1996; Litwin *et al.* 1996; Pincus *et al.* 1996; Wisnewski *et al.* 1996; McDougal *et al.* 1996; Wolfe *et al.* 1996; Jagodzinski *et al.* 1996; Khouri *et al.* 1995; Sullivan *et al.* 1995; Cavacini *et al.* 1995; Posner *et al.* 1995; Turbica *et al.* 1995; Chen *et al.* 1994a; Earl *et al.* 1994; Cavacini *et al.* 1994a; Cavacini *et al.* 1994b; Cook *et al.* 1994; Thali *et al.* 1994; Bagley *et al.* 1994; Marasco *et al.* 1993; Watkins *et al.* 1993; Pincus *et al.* 1993; Klasse *et al.* 1993a; Potts *et al.* 1993; Montefiori *et al.* 1993; Wyatt *et al.* 1993; Cavacini *et al.* 1993b; Cavacini *et al.* 1993a; Posner *et al.* 1993; Moore & Ho 1993; Posner *et al.* 1992a; Posner *et al.* 1992b; Wyatt *et al.* 1992; Marasco *et al.* 1992; Thali *et al.* 1992a; Thali *et al.* 1991; Posner *et al.* 1991
Keywords ADCC, antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, assay development, brain/CSF, coreceptor, complement, enhancing activity, escape, immunoprophylaxis, immunotherapy, immunotoxin, inter-clade comparisons, kinetics, mother-to-infant transmission, mucosal immunity, rate of progression, review, structure, vaccine antigen design, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization

- F105: No neutralization of primary isolates observed (John Moore, pers comm) (**variant cross-recognition or cross-neutralization**)
- F105: NIH AIDS Research and Reference Reagent Program: 857.
- F105: The peptide 12p1 (RINNIPWSEAMM) inhibits direct binding of YU2 gp120 or Env trimer to CD4, CCR5 and MAb 17b in a concentration-dependent allosteric manner. 12p1 is thought to bind to unbound gp120 near the CD4 binding site, with a 1:1 stoichiometry. 12p1 also inhibited MAb F105 binding. presumably because F105 favors an unactivated conformation, but not MAbs 2G12 or b12. The 1:1 stoichiomtry, the fact that the peptide binding site is accessible on the trimer, the non-CD4 like aspect of the binding, and an ability to inhibit viral infection in cell cultures make 12p1 a promising lead for therapeutic design. Biorn *et al.* [2004]
- F105: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- F105: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of CD4BS MAb F105 was decreased by trypsin, but increased by thrombin. Thrombin may increase HIV-induced cell fusion in blood by causing a conformational activating shift in gp120. Ling *et al.* [2004] (**antibody binding site definition and exposure**)

- F105: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. F105 recognized most variants,some from each of the four individuals by gp120 immunoprecipitation. Ohagen *et al.* [2003] (**brain/CSF**, **variant cross-recognition or cross-neutralization**)
- F105: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished. Pantophlet *et al.* [2003a] (**antibody binding site definition and exposure**)
- F105: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- F105: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – while b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, the Abs F105, 19b, and Fab b6 were overall very poor neutralizers. Poignard *et al.* [2003] (**antibody interactions**)
- F105: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs F105, 15e, and IgG1b12 as well as their Fab fragments inhibited CD4-independent binding of the V1/V2 loop-deleted gp120 glycoproteins of R5 HIV-1 isolates ADA, YU2 and JR-FL and to CCR5 in a concentration dependent manner. CD4BS MAbs IgG1b12, F91 and F105 and their Fab counterparts (except for C11, used as a negative control) inhibited CD4-independent JR-FL and YU-2 gp120-CCR5 binding to CCR5-expressing Cf2Th cells and syncytium formation. Raja *et al.* [2003] (**antibody binding site definition and exposure**, **co-receptor**)
- F105: 17b: This paper describes the generation of CD4i MAb E51, that like CD4i MAb 17b, blocks CCR5 binding to sCD4-bound gp120. The substitutions E381R, F383S, R419D I420R, K421D, Q422L, I423S, and Y435S (HXB2 numbering) all severely reduce 17b and E51 binding. All but I423S also diminish CCR5 binding by more than 50%. The mutation F383S also inhibits sCD4 binding and F105 binding, and K421D inhibits F105 binding, but not sCD4. Xiang *et al.* [2003] (**antibody binding site definition and exposure**)
- F105: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- F105: gp120 mutants were used to define the CXCR4 binding site using CXCR4 displayed on paramagnetic proteoliposomes (PMPLs) to reduce non-specific gp120 binding—basic residues in the V3 loop and the β19 strand (RIKQ, positions 419-422) were involved, and deletion of the V1-V2 loops allowed CD4-independent CXCR4 binding—MAbs 17b (CD4i) and F105 (CD4BS) were used to study conformational changes in the mutants—the affinity of ΔV1 and ΔV1-V2 mutants for F105 was comparable to the wildtype—V3 mutants did not affect F105 binding—the K421A mutation in the β19 strand dramatically reduced F105 affinity, consistent with what is known about the F105 epitope. Basmaciogullari *et al.* [2002] (**antibody binding site definition and exposure**)
- F105: This study examined Ab interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-gp41 MAb F240 enhanced the binding of CD4BS MAbs IgG1b12 and F105 to both R5X4 and R5 isolates, but had no effect on neutralization. Anti-V3 MAb B4a1 increased CD4BS MAbs IgG1b12 and F105 to R5X4 virions, but only IgG1b12 binding was increased by B4a1 to the R5 isolate, and neutralization was not impacted. Cavacini *et al.* [2002] (**co-receptor**)
- F105: A modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. Chakrabarti *et al.* [2002] (**vaccine antigen design**)
- F105: Review of NAbs that notes that F105 binds the CD4BS, in combination with other MAbs it can protect some macaques against SHIV infection, and that it has strong ADCC activity. Ferrantelli & Ruprecht [2002] (**ADCC**, **antibody interactions**, **immunoprophylaxis**, **review**)
- F105: HIV-1 gp160δCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160δCT with a reconstituted membrane ten-fold better than the same protein on beads, while such an affinity difference was not seen with F105 and 2G12—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160δCT PLs indistinguishably from gp160δCT expressed on the cell surface. Grundner *et al.* [2002] (**antibody binding site definition and exposure**)
- F105: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d,

F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. The high values suggest surface burial or protein folding and ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)

- F105: A pseudotyping assay showed that an X4 V3 loop peptide could enhance infectivity of X4 virus, R5 and R5X4 V3 loops peptides could enhance infectivity of an R5 virus, and R5X4 peptides could enhance infectivity of an R5X4 virus. Neither R5 nor R5X4 peptides influenced binding of CD4BS MAbs F105 and Ig1Gb12, but did increase binding of CD4i MAb 17b. Ling *et al.* [2002] (**antibody binding site definition and exposure**, **co-receptor**)
- F105: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies. Liu *et al.* [2002] (**immunoprophylaxis**)
- F105: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b] (**antibody binding site definition and exposure**)
- F105: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. Xu *et al.* [2002] (**immunoprophylaxis**, **mother-to-infant transmission**)
- F105: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002] (**vaccine antigen design**)
- F105: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002] (**antibody binding site definition and exposure**)
- F105: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to F105. Kolchinsky *et al.* [2001] (**antibody binding site definition and exposure**)
- F105: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkeys yielded highly pathogenic SHIV KU-1—HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160—substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1—17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. Si *et al.* [2001] (**antibody binding site definition and exposure**)
- F105: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. York *et al.* [2001] (**antibody binding site definition and exposure**)
- F105: A triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the plasma half-life was 7.2 +/- 2.2 days. Baba *et al.* [2000] (**immunoprophylaxis**, **mother-to-infant transmission**)
- F105: Host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5beta or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab. Fortin *et al.* [2000]
- F105: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form,

although F105 was an exception and cannot neutralize either form of MN – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000]

- F105: A mini-review of observations of passive administration of IgG NAbs conferring protection against intervenous or vaginal SHIV challenge, that considers why IgG MAbs might protect against mucosal challenge. Robert-Guroff [2000] (**immunoprophylaxis**, **mucosal immunity**, **review**)
- F105: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000] (**vaccine antigen design**)
- F105: A comparison of 25 gp120 specific, conformation dependent MAbs was done and F105 was used for competition studies – F105 did cross-compete with multiple CD4BS specific MAbs, however most could not neutralize even the autologous NL4-3 strains. Sugiura *et al.* [1999] (**antibody interactions**)
- F105: Immunoprecipitation of gp120 and gp160 expressed from a rec Semliki Forest virus by F105 and IgG1b12 indicated that the SFV expressed HIV-1 Env was folded appropriately – and SVF-HIV-1 Env vaccine gave the strongest anti-HIV-1 Env response in mice, when compared to an HIV-1 Env DNA vaccine and a rgp160 protein. Brand *et al.* [1998] (**vaccine antigen design**)
- F105: Phase I dose escalation study, single dose of 100 or 500 mg/m2 was given to 4 HIV+ patients – sustained levels, no immune response against F105, no toxicity, infused Ab retained function – there was no evidence of anti-HIV-1 activity and virus was not diminished at day 1 or 7, by culture or plasma RNA. Cavacini *et al.* [1998b] (**kinetics**, **immunotherapy**)
- F105: The MAb F240 binds to the immunodominant region of gp41 and enhances infection in the presence of complement – reactivity of F240 is enhanced by preincubation of cells with sCD4 or anti-CD4BS MAb F105. Cavacini *et al.* [1998a] (**antibody interactions**)
- F105: Anti-C1 region MAb 87-135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) Kropelin *et al.* [1998] (**antibody interactions**)
- F105: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) Li *et al.* [1998] (**antibody interactions**)
- F105: F105 enhances viral entry of viruses carrying the YU2 envelope glycoproteins, but neutralizes HXBc2. Sullivan *et al.* [1998a] (**enhancing activity**)
- F105: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. Wyatt *et al.* [1998] (**antibody binding site definition and exposure**, **structure**)
- F105: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to a CD4BS MAb, F105 or sCD4. Cao *et al.* [1997b] (**antibody binding site definition and exposure**)
- F105: In a multilaboratory blinded study, failed to neutralize any of nine B clade primary isolates. D'Souza *et al.* [1997] (**variant cross-recognition or cross-neutralization**)
- F105: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – F105 could only achieve 50% neutralization alone – all Ab combinations tested showed synergistic neutralization – F105 has synergistic response with MAbs 694/98-D (anti-V3), 48d, 2F5, and 2G12, and also with HIVIG. Li *et al.* [1997] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- F105: Neutralizes TCLA strains, but not primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- F105: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-93, are deleted. Wyatt *et al.* [1997] (**antibody binding site definition and exposure**)
- F105: Intracellular co-expression of heavy and light chains of the Fab105 fragment MAb F105 was enhanced by inclusion of an internal ribosome entry site (IRES) sequence – the Fab105 IRES expression cassette was cloned into an adeno-associated virus (AAV) shuttle vector, and transduced into human lymphocytes which were able to produce and secrete the Fab105 fragments while maintaining normal growth – several primary HIV-1 patient isolates were effectively blocked. Chen *et al.* [1996] (**immunotherapy**)
- F105: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop results in less potent inhibition of F105 binding by CRDS – binding site of F105 described as 256-257 ST, 368-370 DPE, 421 K, and 470-484 PGGGDMRDNWRSELY. Jagodzinski *et al.* [1996] (**antibody binding site definition and exposure**)
- F105: Binding of F105 to oligomeric gp120 occurs despite the fact it cannot neutralize primary isolates. Litwin *et al.* [1996]
- F105: Neutralizes HIV-1 LAI less potently than V3 specific MAbs. McDougal *et al.* [1996]
- F105: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. Pincus *et al.* [1996] (**immunotoxin**)
- F105: F105 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- F105: Phase I study – MAb clearance in plasma has a 13 day half-life. Wolfe *et al.* [1996] (**kinetics**, **immunotherapy**)

- F105: Changing heavy chain from IgG1 to IgG3 increased neutralization efficiency. Cavacini *et al.* [1995]
- F105: Biotinylated F105 was used for competition studies with Ab derived from pregnant HIV-1 + women – a correlation between maternal anti-CD4 BS Abs overlapping the F105 binding site and lack of HIV-1 transmission to infants was noted. Khouri *et al.* [1995] (**mother-to-infant transmission**)
- F105: Eight patient phase Ia trial for use as an immunotherapeutic – no clinical or biochemical side effects observed, plasma levels of 10 ug/ml maintained for 21 days. Posner *et al.* [1995] (**immunotherapy**)
- F105: Efficient neutralization of T-cell adapted lines HXBc2 and MN, no neutralization of primary isolates 89.6, ADA and YU2 – even some enhancement of infection of ADA and YU2 was observed. Sullivan *et al.* [1995] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- F105: An immunoassay for titrating CD4BS serum antibody was developed using a gp120-coated solid phase and competition with MAb F105 – 109/110 French HIV-1 + sera and 51/56 HIV-1 + African sera had detectable CD4BS Abs using this assay, demonstrating CD4 binding site conservation among diverse subtypes – CD4BS Abs were detected soon after seroconversion and persisted – 0/21 HIV-2 + sera reacted, indicating that the HIV-1 and HIV-2 CD4BS Abs are not cross-reactive. Turbica *et al.* [1995] (**assay development**, **inter-clade comparisons**)
- F105: Comparison of MAb F105 sequences with those of MAbs 21h and 15e. Bagley *et al.* [1994] (**antibody sequence, variable domain**)
- F105: Administered intravenously to four cynomologus monkeys, plasma pharmacokinetics and biological activity tested. Cavacini *et al.* [1994b] (**kinetics**)
- F105: Fab fragments show reduced capacity to neutralize IIIB, MN, and RF compared to intact IgG1, suggesting bivalent interaction may be important in binding and neutralization. Cavacini *et al.* [1994a] (**variant cross-recognition or cross-neutralization**)
- F105: A human CD4+ T lymphocyte line was transduced to express Fab fragments of F105 – heavy and light chains are joined by an inter-chain linker – in the transduced cells infected with HIV-1, the Fab binds intracellularly to the envelope protein and inhibits HIV-1 production – secreted Fab fragments neutralize cell-free HIV-1– combined intra- and extracellular binding activities of the expressed Fab make transduced cells resistant to HIV-1 infection and also can protect surrounding lymphocytes by secreting neutralizing antibodies. Chen *et al.* [1994a]; Marasco *et al.* [1993] (**variant cross-recognition or cross-neutralization**)
- F105: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – anti-CD4 MAbs moderately inhibit gp120 binding to GalCer, possibly through steric hindrance – binding of GalCer to gp120 inhibited but did not completely block F105 binding. Cook *et al.* [1994] (**brain/CSF**)
- F105: Used as a positive control for CD4 BS antibodies in a study of the influence of oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994] (**antibody binding site definition and exposure**)
- F105: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs 48d, 21h, 15e and 17b) Thali *et al.* [1994] (**antibody binding site definition and exposure**)
- F105: Additive MN or SF2 neutralization when combined with anti-V3 MAbs 447-52D and 257-D. Cavacini *et al.* [1993a] (**antibody interactions**)
- F105: Serum from all asymptomatic HIV-1 positive people tested block F105 binding, but only from 27% of symptomatic individuals. Cavacini *et al.* [1993b] (**rate of progression**)
- F105: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – required >81 fold higher concentrations to neutralize the mutant than wild type. Klasse *et al.* [1993a] (**antibody interactions**)
- F105: Study of synergy between F105 and sera from vaccinated volunteers with V3-loop specific neutralization activity – 2/3 sera demonstrated neutralization synergy, and 3/3 binding/fusion-inhibition synergy. Montefiori *et al.* [1993] (**antibody interactions**)
- F105: Called F-105 – neutralizes IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120. Moore & Ho [1993]
- F105: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – F105 was used as a control – infected lab workers and some of the gp160 vaccinees had a MAb response that could inhibit gp120-CD4 binding, at lower titers than the infected lab workers. Pincus *et al.* [1993] (**vaccine-specific epitope characteristics**)
- F105: F105 binds to and neutralizes selected lab strains and 3/9 HIV-1 primary isolates – synergistic enhancement of neutralization by seropositive sera. Posner *et al.* [1993] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- F105: Study of synergy of neutralization and binding comparing F105 and sCD4 with the V3 MAbs: 50.1, 59.1, 83.1, and 58.2 – synergy was observed, and the data suggest that binding of one ligand (F105) can increase the binding of the second (e. g. V3 loop MAbs) due to conformational changes. Potts *et al.* [1993] (**antibody interactions**)
- F105: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – F105 neutralization was not affected by this mutation. Watkins *et al.* [1993] (**escape**)
- F105: Binding to Delta V1/2 and Delta V1/2/3 mutant glycoproteins is 2.4- and 13-fold greater, respectively, than binding to wildtype gp120. Wyatt *et al.* [1993] (**antibody binding site definition and exposure**)
- F105: MAb cDNA sequence – V H4 V71-4 rearranged with a D H D-D fusion product of dlr4 and da4, and with J H5 – V kappa is from the Humvk325 germline gene joined with Jkappa 2. Marasco *et al.* [1992] (**antibody sequence, variable domain**)
- F105: F105 mediates ADCC against SF2 through the CD16+ population of PBMC – does not mediate complement-dependent cytotoxicity. Posner *et al.* [1992b] (**ADCC**, **complement**)
- F105: Significant enhancement of F105 binding to RF infected cells preincubated with V3-specific MAbs V3-2 and V3-1. Posner *et al.* [1992a] (**antibody interactions**)

- F105: Amino acid substitutions that impair F105 neutralization inhibit gp120-CD4 interaction. Thali *et al.* [1992a] (**antibody binding site definition and exposure**)
- F105: Precipitation of Delta 297-329 env glycoprotein, which has a deleted V3 loop, is much more efficient than precipitation of wild type. Wyatt *et al.* [1992] (**antibody binding site definition and exposure**)
- F105: First description of F105, binds topographically near the CD4-binding site – inhibits binding of free, infectious virions to uninfected HT-H9 cells, but does not react with virus adsorbed to uninfected HT-H9 cells – soluble rCD4 pre-bound to infected cells inhibits F105 binding – F105 inhibits infection of HT-H9 cells in standard neutralization assays with HIV-1 and MN strains. Posner *et al.* [1991] (**antibody binding site definition and exposure**, **antibody generation**)
- F105: F105 neutralization escape mutants result from changes in amino acids in discontinuous regions: C2, 256-262 and C3, 386-370. Thali *et al.* [1991] (**antibody binding site definition and exposure**)

No. 1031
MAb ID F91 (F-91)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen
Species (Isotype)
Ab Type CD4BS
Research Contact James Robinson, University of Connecticut, Storrs
References Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Raja *et al.* 2003; Pantophlet *et al.* 2003a; Kwong *et al.* 2002; Xiang *et al.* 2002b; Yang *et al.* 2002; Yang *et al.* 2000; Fouts *et al.* 1998; Binley *et al.* 1998; Parren *et al.* 1998a; Mondor *et al.* 1998; Fouts *et al.* 1997; Moore & Sodroski 1996; Moore *et al.* 1994b; Moore & Ho 1993
Keywords antibody binding site definition and exposure, antibody interactions, co-receptor, interclade comparisons, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- F91: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- F91: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished. Pantophlet *et al.* [2003a] (**antibody binding site definition and exposure**)
- F91: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- F91: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs F105, 15e, and IgG1b12 as well as their Fab fragments inhibited CD4-independent binding of the V1/V2 loop-deleted gp120 glycoproteins of R5 HIV-1 isolates ADA, YU2 and JR-FL and to CCR5 in a concentration dependent manner. CD4BS MAbs IgG1b12, F91 and F105 and their Fab counterparts (except for C11, used as a negative control) inhibited CD4-independent JR-FL and YU-2 gp120-CCR5 binding to CCR5-expressing Cf2Th cells and syncytium formation. Raja *et al.* [2003] (**co-receptor**)
- F91: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- F91:Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- F91: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope –

another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b] (**antibody binding site definition and exposure**)

- F91: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002] (**antibody binding site definition and exposure**)
- F91: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000] (**antibody binding site definition and exposure**)
- F91: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type. Binley *et al.* [1998] (**antibody binding site definition and exposure**)
- F91: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer – conclusions of this paper contrast with Parren *et al.* [1998a] Fouts *et al.* [1998]. Fouts *et al.* [1998]; Parren *et al.* [1998a] (**antibody binding site definition and exposure**)
- F91: Weak inhibition of binding of Hx10 to CD4 positive or negative cells, weakly neutralizing. Mondor *et al.* [1998]
- F91: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**antibody binding site definition and exposure**)
- F91: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – F91 bound monomer, did not bind oligomer or neutralize JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- F91: Unusual pattern of reciprocal enhancement with several anti-V2 and V3 directed MAbs – reciprocal inhibition of other CD4BS MAbs. Moore & Sodroski [1996] (**antibody binding site definition and exposure**, **antibody interactions**)
- F91: Has strong cross-reactivity with gp120 monomers from most subtypes, A-F. Moore *et al.* [1994b] (**inter-clade comparisons**)
- F91: Called F-91 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120. Moore & Ho [1993] (**variant cross-recognition or cross-neutralization**)

No. 1032
MAb ID FG39
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Zwick *et al.* 2003
Keywords antibody interactions

- FG39: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4BS Fab first used in this study. Zwick *et al.* [2003] (**antibody interactions**)

No. 1033
MAb ID Fbb14
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Zwick *et al.* 2003
Keywords antibody interactions

- Fbb14: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4BS Fab first used in this study. Fbb14 was unusual among CDBS Abs in that it didn't enhance 4KG5's binding, like b12, but it did not inhibit it either as the other 13 CD4BS Abs did, it remained neutral. Zwick *et al.* [2003] (**antibody interactions**)

No. 1034
MAb ID GP13 (ARP3054)
HXB2 Location Env
Author Location gp120

Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Vella *et al.* 2002; Schutten *et al.* 1997; Schutten *et al.* 1996; Wisnewski *et al.* 1996; Bolmstedt *et al.* 1996; Schutten *et al.* 1995b; Schutten *et al.* 1995a; Bagley *et al.* 1994; Back *et al.* 1993; Schutten *et al.* 1993
Keywords antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, assay development, binding affinity, enhancing activity, escape, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- GP13: UK Medical Research council AIDS reagent: ARP3054.
- GP13: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- GP13: Called ARP3054: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. Vella *et al.* [2002] (**assay development**)
- GP13: Neutralized (50%) an SI-env chimeric virus and enhanced (>5 fold) an NSI-env chimeric virus. Schutten *et al.* [1997] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- GP13: Sera were obtained from guinea pigs vaccinated either with gp160, or with gp160 lacking N-linked glycans at N406, N448, and N463 – these sera could block equally well both the CD4 BS MAb GP13 and the V3 MAb F58/H3. Bolmstedt *et al.* [1996] (**antibody interactions**)
- GP13: IIIB neutralizing MAbs *in vitro* fail to neutralize in a mouse model *in vivo*. Schutten *et al.* [1996]
- GP13: GP13 is V H5 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- GP13: Neutralizes IIIB – only slight inhibition of SI phenotype, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor. Schutten *et al.* [1995a] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- GP13: Neutralizes T-cell adapted viruses but not the SI strain 16.2, despite high binding affinity. Schutten *et al.* [1995b] (**variant cross-recognition or cross-neutralization**, **binding affinity**)
- GP13: Mutations in a neutralization resistant isolate obtained by passage of the IIIB isolate in chimpanzees reduced neutralization, but the escape was not as clear as seen with anti-V3 MAbs. Back *et al.* [1993] (**escape**)
- GP13: Neutralized a broad range of HIV-1 strains from phylogenetically different subfamilies – the following gp120 amino acid substitutions strongly inhibit binding: 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q or D), 384(Y/E) Schutten *et al.* [1993] (**antibody binding site definition and exposure**, **inter-clade comparisons**)

No. 1035
MAb ID GP44
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Wisnewski *et al.* 1996; Bagley *et al.* 1994; Schutten *et al.* 1993
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review, variant cross-recognition or cross-neutralization

- GP44: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- GP44: GP44 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- GP44: Exhibited a more restricted pattern of neutralizing activity than GP13 and GP68 – the following gp120 amino acid substitutions strongly inhibit binding: 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q or D) Schutten *et al.* [1993] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

No. 1036
MAb ID GP68
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Guillon *et al.* 2002b; Wisnewski *et al.* 1996; Schutten *et al.* 1995a; Bagley *et al.* 1994; Klasse *et al.* 1993a; Schutten *et al.* 1993
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, enhancing activity, review, variant cross-recognition or cross-neutralization

- GP68: UK Medical Research Council AIDS reagent: ARP3055.
- GP68: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)

- GP68: The affect of Ab binding on infectivity was studied by pseudotyping three related envs with different phenotypes – R5 viruses were preferentially enhanced, not X4 – the V3 region was the main determinant of Ab-mediated enhancement and modulation of the interaction between CCR5 and gp120 is critical – tests with MAbs anti-V3 391/95-D and CD4BS-specific GP68 indicate that Ab specificity did not determine whether or not infectivity was enhanced or neutralized, rather the phenotype was determined by Envelope conformation. Guillon *et al.* [2002b] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- GP68: GP68 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- GP68: Neutralizes IIIB – only slight inhibition of SI phenotype, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor. Schutten *et al.* [1995a] (**variant cross-recognition or cross-neutralization**)
- GP68: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – GP68 required markedly higher concentrations to neutralize the mutant than wild type. Klasse *et al.* [1993a] (**antibody binding site definition and exposure**)
- GP68: Neutralized a broad range of HIV-1 lab strains from phylogenetically different subfamilies – the following gp120 amino acid substitutions strongly inhibit binding: 117(K/W), 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q), 384(Y/E), 435(Y/H) Schutten *et al.* [1993] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

No. 1037
MAb ID HF1.7
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen anti-idiotype
Species (Isotype) mouse (IgM)
Ab Type CD4BS
References Chanh *et al.* 1987

- HF1.7: An anti-Id antibody stimulated by anti-CD4 MAb Leu-3a binds to recombinant gp160, suggesting HF1.7 mimics CD4. Chanh *et al.* [1987]

No. 1038
MAb ID HT5 (205-43-1)
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing L (weak)
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
Research Contact Ciba-Geigy AG (Basel, Switzerland), and Tanox Biosystems, Houston, Texas
References Pugach *et al.* 2004; Gorny & Zolla-Pazner 2004; Herrera *et al.* 2003; Grovit-Ferbas *et al.* 2000; Parren *et al.* 1998a; Fouts *et al.* 1998; Fouts *et al.* 1997; Moore *et al.* 1995a; Moore *et al.* 1994b
Keywords reversion, viral fitness, variant cross-recognition or cross-neutralization

- HT5: Also called 205-43-1. This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004]
- HT5: Called 205-43-1: A primary isolate, CC1/85, was passaged 19 times in PBMC and gradually acquired increased sensitivity to FAb b12 and sCD4 that was attributed to changes in the the V1V2 loop region, in particular the loss of a potential glycosylation site. The affinity for sCD4 was unchanged in the monomer, suggesting that the structural impact of the change was manifested at the level of the trimer. The passaged virus, CCcon19, retained an R5 phenotype and its neutralization susceptibility to other Abs was essentially the same as CC1/85. Three CD4BS MAbs, 205-46-9, 205-42-15, and 205-43-1, did not neutralize either the primary or passaged variant. Pugach *et al.* [2004] (**reversion, viral fitness**, **variant cross-recognition or cross-neutralization**)
- HT5: Called 205-43-1 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution. Herrera *et al.* [2003]
- HT5: Called 205-43-1: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. Grovit-Ferbas *et al.* [2000]
- HT5: HT5, HT6, and HT7 are also known as 205-43-1, 205-42-15, and 205-46-9, respectively. Rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2. Fouts *et al.* [1998]
- HT5: HT5 and HT6 bind JRSF oligomer but with low affinity, and are not neutralizing – conclusions of this paper contrast with Parren *et al.* [1998a] Fouts *et al.* [1998]. Fouts *et al.* [1998]; Parren *et al.* [1998a]
- HT5: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL. Fouts *et al.* [1997]

- HT5: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only weakly neutralizes IIIB and MN. Moore *et al.* [1995a]
- HT5: 205-46-9 was cross-reactive across clades A-F, 205-43-1 very cross-reactive but not quite as extensive 205-46-9. Moore *et al.* [1994b]

No. 1039
MAb ID HT6 (205-42-15)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (weak)
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
Research Contact Ciba-Geigy AG Basel, Switzerland, and Tanox Biosystems, Houston, Texas
References Pugach *et al.* 2004; Gorny & Zolla-Pazner 2004; Herrera *et al.* 2003; Parren *et al.* 1998a; Fouts *et al.* 1998; Fouts *et al.* 1997; Moore *et al.* 1995a; Moore *et al.* 1994b
Keywords antibody binding site definition and exposure, antibody interactions, inter-clade comparisons, reversion, viral fitness, review, variant cross-recognition or cross-neutralization

- HT6: Called 205-42-15: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- HT6: Called 205-42-15: A primary isolate, CC1/85, was passaged 19 times in PBMC and gradually acquired increased sensitivity to FAb b12 and sCD4 that was attributed to changes in the the V1V2 loop region, in particular the loss of a potential glycosylation site. The affinity for sCD4 was unchanged in the monomer, suggesting that the structural impact of the change was manifested at the level of the trimer. The passaged virus, CCcon19, retained an R5 phenotype and its neutralization susceptibility to other Abs was essentially the same as CC1/85. Three CD4BS MAbs, 205-46-9, 205-42-15, and 205-43-1, did not neutralize either the primary or passaged variant. Pugach *et al.* [2004] (**reversion, viral fitness**, **variant cross-recognition or cross-neutralization**)
- HT6: Called 205-42-15: CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution. Herrera *et al.* [2003] (**antibody binding site definition and exposure**, **antibody interactions**)
- HT6: HT5, HT6, and HT7 are also known as 205-43-1 , 205-42-15, and 205-46-9, respectively. Fouts *et al.* [1998]
- HT6: HT5 and HT6 bind JRSF oligomer but with low affinity, and are not neutralizing – conclusions of this paper contrast with Parren *et al.* [1998a] Fouts *et al.* [1998]. Fouts *et al.* [1998]; Parren *et al.* [1998a] (**antibody binding site definition and exposure**)
- HT6: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**, **antibody interactions**)
- HT6: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only weakly neutralizes IIIB and MN. Moore *et al.* [1995a] (**variant cross-recognition or cross-neutralization**)
- HT6: 205-46-9 was cross-reactive across clades A-F, 205-43-1 was not quite as extensively cross-reactive. Moore *et al.* [1994b] (**inter-clade comparisons**)

No. 1040
MAb ID HT7 (205-46-9)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (IIIB)
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
Research Contact Ciba-Geigy AG (Basel, Switzerland), and Tanox Biosystems, Houston, Texas
References Pugach *et al.* 2004; Gorny & Zolla-Pazner 2004; Herrera *et al.* 2003; Grovit-Ferbas *et al.* 2000; Parren *et al.* 1998a; Fouts *et al.* 1998; Fouts *et al.* 1997; Moore *et al.* 1995a; Moore *et al.* 1994b
Keywords antibody binding site definition and exposure, assay standardization/improvement, inter-clade comparisons, reversion, viral fitness, review, variant cross-recognition or cross-neutralization

- HT7: Also called 205-46-9. This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- HT7: Called 205-46-9: A primary isolate, CC1/85, was passaged 19 times in PBMC and gradually acquired increased sensitivity to FAb b12 and sCD4 that was attributed to changes in the V1V2 loop region, in particular the loss of a potential glycosylation site. The affinity for sCD4 was unchanged in the monomer, suggesting that the structural impact of the change was manifested at the level of the trimer. The passaged virus, CCcon19, retained an R5 phenotype and its neutralization susceptibility to other Abs was essentially the same as CC1/85. Three CD4BS MAbs, 205-46-9, 205-42-15, and 205-43-1, did not neutralize either the primary or passaged variant. Pugach *et al.* [2004] (**reversion, viral fitness**, **variant cross-recognition or cross-neutralization**)
- HT7: Called 205-46-9 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutral-

izing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution. Herrera *et al.* [2003] (**antibody binding site definition and exposure**)

- HT7: Called 205-46-9. To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. Grovit-Ferbas *et al.* [2000] (**antibody binding site definition and exposure**)
- HT7: Called 205-46-9. HT5, HT6, and HT7 are also known as 205-43-1 , 205-42-15, and 205-46-9, respectively. Binds JRSF oligomer with high affinity as does IgG1b12, but IgG1b12 is neutralizing, 205-46-9 is not – conclusions of this paper contrast with Parren98 – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect – rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2. Fouts *et al.* [1998] (**assay standardization/improvement**)
- HT7: Binds JRSF oligomer with high affinity, at least as high as IgG1b12, but IgG1b12 is neutralizing, H7 is not – conclusions of this paper contrast with Parren *et al.* [1998a] – authors propose a model where H7 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect Fouts *et al.* [1998]. Fouts *et al.* [1998]; Parren *et al.* [1998a] (**antibody binding site definition and exposure**)
- HT7: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- HT7: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only neutralizes IIIB well, with sporadic weak neutralization of other isolates. Moore *et al.* [1995a] (**variant cross-recognition or cross-neutralization**)
- HT7: 205-46-9 was cross-reactive across clades A-F, 205-43-1 was cross-reactive, but not quite as extensive. Moore *et al.* [1994b] (**inter-clade comparisons**)

No. 1041
MAb ID ICR 39.13g (ICR39.13g, 39.13g)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2b)
Ab Type CD4BS
Research Contact Jackie Cordell and C. Dean
References Vella *et al.* 2002; Peet *et al.* 1998; Klasse & Sattentau 1996; Armstrong & Dimmock 1996; McKeating *et al.* 1996; Beretta & Dalgleish 1994; McLain & Dimmock 1994; Klasse *et al.* 1993a; Thali *et al.* 1993; Moore & Ho 1993; McKeating *et al.* 1993b; McKeating *et al.* 1992c; McKeating *et al.* 1992a; Cordell *et al.* 1991

- ICR 39.13g: UK Medical Research Council AIDS reagent: ARP390.
- ICR 39.13g: Called ARP390/391, but no such entry was found at the UK Medical Research Council AIDS reagent web site: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. Vella *et al.* [2002]
- ICR 39.13g: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – ICR 39.13g was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]
- ICR 39.13g: Post-attachment neutralization mechanism, in contrast to MAb 39.3b. Armstrong & Dimmock [1996]
- ICR 39.13g: Variants of LAI have differing neutralization susceptibility to 39.13g. Klasse & Sattentau [1996]
- ICR 39.13g: Called 39.13g Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. McKeating *et al.* [1996]
- ICR 39.13g: Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively – mediates neutralization with 2.3 molecules of IgG. McLain & Dimmock [1994]
- ICR 39.13g: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – ICR 39.13g required moderately higher concentrations to neutralize the mutant than wild type. Klasse *et al.* [1993a]
- ICR 39.13g: Neutralization activity against HXB10, RF, SF-2 and MN strains of HIV-1. McKeating *et al.* [1993b]
- ICR 39.13g: Conformational, does not bind denatured gp120 – weak neutralization of IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120. Moore & Ho [1993]
- ICR 39.13g: Strongly inhibits CD4 inducible MAb 48d. Thali *et al.* [1993]
- ICR 39.13g: Binds to a conformational epitope involved in CD4 binding – exerts a synergistic effect in combination with V3 directed MAbs. McKeating *et al.* [1992a]
- ICR 39.13g: Cross-competes with MAbs ICR 39.3b and 15e. Cordell *et al.* [1991]

No. 1042
MAb ID ICR 39.3b (39.3, 39.3b, ICR39.3b)

HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2b)
Ab Type CD4BS
Research Contact J. Cordell and C. Dean
References Wyatt *et al.* 1998; Jeffs *et al.* 1996; Armstrong & Dimmock 1996; McLain & Dimmock 1994; Moore *et al.* 1993b; Moore & Ho 1993; McKeating *et al.* 1992c; Cordell *et al.* 1991

- ICR 39.3b: also known as 39.3, 39.3b and ICR39.3b.
- ICR 39.3b: UK Medical Research Council AIDS reagent: ARP391.
- ICR 39.3b: Called 39.3 – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. Wyatt *et al.* [1998]
- ICR 39.3b: Neutralizes only if the antibody is added prior to the attachment of the virus to the cell, in contrast to 39.13g. Armstrong & Dimmock [1996]
- ICR 39.3b: Called 39.3b – increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. Jeffs *et al.* [1996]
- ICR 39.3b: Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively. McLain & Dimmock [1994]
- ICR 39.3b: Conformational, does not bind to denatured IIIB. Moore & Ho [1993]
- ICR 39.3b: Cross-competes with MAbs ICR 39.13g and 15e. Cordell *et al.* [1991]

No. 1043
MAb ID Ia3
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Zwick *et al.* 2003
Keywords antibody interactions

- Ia3: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4BS Fab first used in this study. Zwick *et al.* [2003] (**antibody interactions**)

No. 1044
MAb ID Ia7
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Zwick *et al.* 2003
Keywords antibody interactions

- Ia7: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4BS Fab first used in this study. Zwick *et al.* [2003] (**antibody interactions**)

No. 1045
MAb ID IgG1b12 (Fab b12, Fab 3B3, MAb IgG1b12, IgG1-b12, IgG1 b12, IgGB12, b4/12)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact D. Burton, Scripps Research Institute, La Jolla, CA, also J. Geltowsky and J. Pyati, R. W. Johnson Pharmaceutical Resear
References Safrit *et al.* 2004; Pugach *et al.* 2004; Pinter *et al.* 2004; Nabatov *et al.* 2004; McCaffrey *et al.* 2004; Jeffs *et al.* 2004; Biorn *et al.* 2004; Zwick *et al.* 2004; Zwick *et al.* 2003; Pantophlet *et al.* 2003b; Zhu *et al.* 2003; Veazey *et al.* 2003; Montefiori *et al.* 2003; Kitabwalla *et al.* 2003; Zhang *et al.* 2003; Wang 2003; Mascola 2003; Raja *et al.* 2003; Hart *et al.* 2003; Ferrantelli *et al.* 2003; Dey *et al.* 2003; Cavacini *et al.* 2003; Binley *et al.* 2003; Herrera *et al.* 2003; Pantophlet *et al.* 2003a; Poignard *et al.* 2003; Ling *et al.* 2002; Lewis *et al.* 2002; Kwong *et al.* 2002; Gorry *et al.* 2002; Cavacini *et al.* 2002; Bures *et al.* 2002; Liu *et al.* 2002; Ferrantelli & Ruprecht 2002; Klasse & Sattentau 2002; Zhang *et al.* 2002; Grundner *et al.* 2002; Edwards *et al.* 2002; Xiang *et al.* 2002b; Vella *et al.* 2002; Chakrabarti *et al.* 2002; Xu *et al.* 2002; Scanlan *et al.* 2002; Saphire *et al.* 2002; Yang *et al.* 2002; Schulke *et al.* 2002; Sanders *et al.* 2002; Golding *et al.* 2002b; Srivastava *et al.* 2002; Hezareh *et al.* 2001; Xu *et al.*

2001; Hofmann-Lehmann *et al.* 2001; Verrier *et al.* 2001; Spenlehauer *et al.* 2001; Zeder-Lutz *et al.* 2001; Poignard *et al.* 2001; Parren *et al.* 2001; Zwick *et al.* 2001c; Zwick *et al.* 2001b; Zwick *et al.* 2001a; York *et al.* 2001; Yang *et al.* 2001; Saphire *et al.* 2001b; Saphire *et al.* 2001a; Kolchinsky *et al.* 2001; Si *et al.* 2001; Park *et al.* 2000; Nyambi *et al.* 2000; Ly & Stamatatos 2000; Grovit-Ferbas *et al.* 2000; Binley *et al.* 1999; Beddows *et al.* 1999; Giraud *et al.* 1999; Montefiori & Evans 1999; Hioe *et al.* 1999; Jackson *et al.* 1999; Crawford *et al.* 1999; Poignard *et al.* 1999; Stamatatos & Cheng-Mayer 1998; Kropelin *et al.* 1998; Frankel *et al.* 1998; Sullivan *et al.* 1998a; Schonning *et al.* 1998; Brand *et al.* 1998; Parren *et al.* 1998b; Takefman *et al.* 1998; Fouts *et al.* 1998; Binley *et al.* 1998; Connor *et al.* 1998; Parren *et al.* 1998a; Mondor *et al.* 1998; Wyatt *et al.* 1998; Valenzuela *et al.* 1998; Parren & Burton 1997; Parren *et al.* 1997a; Parren *et al.* 1997b; Boots *et al.* 1997; Burton & Montefiori 1997; Wyatt *et al.* 1997; Ugolini *et al.* 1997; Ditzel *et al.* 1997; Stamatatos *et al.* 1997; Moore & Trkola 1997; Kessler II *et al.* 1997; Li *et al.* 1997; Fouts *et al.* 1997; Mo *et al.* 1997; Schutten *et al.* 1997; D'Souza *et al.* 1997; McKeating 1996; Sattentau 1996; Trkola *et al.* 1996a; Poignard *et al.* 1996a; Poignard *et al.* 1996b; Gauduin *et al.* 1996; Moore & Sodroski 1996; Yang *et al.* 1997c; Sullivan *et al.* 1995; Ditzel *et al.* 1995; Trkola *et al.* 1995; Parren *et al.* 1995; Moore & Ho 1995; Moore *et al.* 1995a; Sattentau 1995; Sattentau *et al.* 1995; Kessler *et al.* 1995; Moore *et al.* 1994b; Burton *et al.* 1994; Roben *et al.* 1994; Barbas III *et al.* 1992; Burton *et al.* 1991

Keywords ADCC, antibody binding site definition and exposure, antibody generation, antibody interactions, assay development, assay standardization/improvement, binding affinity, co-receptor, complement, enhancing activity, escape, immunoprophylaxis, immunotherapy, inter-clade comparisons, kinetics, mimotopes, mother-to-infant transmission, mucosal immunity, responses in children, reversion, viral fitness, review, structure, vaccine antigen design, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization

- IgG1b12: Fab b12 was derived from IgG1b12, Fab 3B3 was derived from Fab b12 by random mutagenesis and selected for increased affinity to sgp120 – database note. (**antibody generation**)
- IgG1b12: UK Medical Research Council AIDS reagent: ARP3065.
- IgG1b12: NIH AIDS Research and Reference Reagent Program: 2640IgG1b12 was more effective than 2G12 and 2F5 in neutralizing 5/8 south african and 4/8 malawian clade C primary HIV-1 isolates in a p24 ELISA capture assay. (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- IgG1b12: Called b12. The peptide 12p1 (RINNIPWSEAMM) inhibits direct binding of YU2 gp120 or Env trimer to CD4, CCR5 and MAb 17b in a concentration-dependent allosteric manner. 12p1 is thought to bind to unbound gp120 near the CD4 binding site, with a 1:1 stoichiometry. 12p1 also inhibited MAb F105 binding. presumably because F105 favors an unactivated conformation, but not 2G12 or b12. The 1:1 stoichiomtry, the fact that the peptide binding site is accessible on the trimer, the non-CD4 like aspect of the binding, and an ability to inhibit viral infection in cell cultures make it a promising lead for therapeutic design. Biorn *et al.* [2004]
- IgG1b12: Called b12. A set of oligomeric envelope proteins were made from six primary isolates for potenial use as vaccine antigens: 92/UG/037 (clade A), HAN2/2 (clade B), 92/BR25/025 (clade C), 92/UG/021 (clade D), 93/BR/029 (clade F) and MVP5180 (clade O). This was one of a panel of MAbs used to explore folding and exposure of well characterized epitopes. The clade C isolate BR25 is apparently misfolded, as conformation-dependent antibodies did not bind to it. b12 bound to clade A, B, D and F HIV-1 primary isolates. Polyclonal sera raised in rabbits against these antigens cross-bound the other antigens, but none of the sera had neutralizing activity. Jeffs *et al.* [2004] (**vaccine antigen design**, **inter-clade comparisons**)
- IgG1b12: Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The loss of the any of the five glycans, within the V3 loop (GM299 V3), C2 (GM292 C2), C3 (GM329 C3), C4 (GM438 C4), or V5 (GM454 V5) made SF162 become more sensitive to IgG1b12 neutralization. V3 glycans tended to shield V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans shielded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- IgG1b12: Called b12. A set of HIV-1 chimeras that altered V3 net charge and glycosylation patterns in V1V2 and V3, involving inserting V1V2 loops from a late stage primary isolate taken after the R5 to X4 switch, were studied with regard to phenotype, co-receptor usage, and MAb neutralization. The loops were cloned into a HXB2 envelope with a LAI viral backbone. It was observed that the addition of the late-stage isolate V1V2 region and the loss of V3-linked glycosylation site in the context of high positive charge gave an X4 phenotype. R5X4 viruses were more sCD4 and 2G12 neutralization resistant than either R5 or X4, but the opposite pattern was observed for b12. Addition of the late stage V1V2 altered neutralization for both MAbs, but this alteration was reversed with the loss of the V3 glycan. Nabatov *et al.* [2004] (**antibody binding site definition and exposure**, **co-receptor**)
- IgG1b12: Called IgG-b12. V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162.

JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12 which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. Three anti-CD4BS MAbs were tested, including IgG1b12 which neutralizes both JRFL and SF162. The affinities for IgG1b12 and 5145A were similar for both JRFL and SF612, but 1125A bound with 2.5 fold higher affinity to SF162. 5145A and 1125H both preferentially neutralize SF162, but not JRFL, and the CD4BS is more sensitive to neutralization in the context of the SF162 V1V2 loop. This was also true for neutralization by sCD4. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)

- IgG1b12: Called b12. A primary isolate, CC1/85, was passaged 19 times in PBMC and gradually acquired increased sensitivity to FAb b12 and sCD4 that was attributed to changes in the V1V2 loop region, in particular the loss of a potential glycosylation site. The affinity for sCD4 was unchanged in the monomer, suggesting that the structural impact of the change was manifested at the level of the trimer. The passaged virus, CCcon19, retained an R5 phenotype and its neutralization susceptibility to other Abs was essentially the same as CC1/85. CCcon19 (IC50 0.3) was significantly more senstivie to neutralization by b12 than was CC1/85 (IC50 6.0). Pugach *et al.* [2004] (**reversion, viral fitness**, **variant cross-recognition or cross-neutralization**)
- IgG1b12: This review discusses research presented at the Ghent Workshop of prevention of breast milk transmission and immunoprophylaxis for HIV-1 in pediatrics (Seattle, Oct. 2002), and makes the case for developing passive or active immunoprophylaxis in neonates to prevent mother-to-infant transmission. Macaque studies have shown that passive transfer of NAb combinations (for example, IgG1b12, 2G12, 2F5, and 4E10) can confer partial or complete protection to infant macaques from subsequent oral SHIV challenge. Safrit *et al.* [2004] (**immunoprophylaxis**, **mother-to-infant transmission**)
- IgG1b12: Called IgG1 b12. This paper is a study of the 2F5 NAb complexed to peptide ELDKWAS; the peptide was found to interact with amino acids near the base of the very long (22 residue) CDR 3H region of the Ab, although a Phe at the apex of the loop was also important. The authors suggest that particularly long CDR H3 regions may be a common feature of HIV-1 neuturalizing antibodies – there are 22 residues in 2F5's H3, 18 in IgG1b12's H3, and 22 residues in X5's H3. They express concern that because small animals like mice are unable to elicit Ab responses with such long H3s, they may be poor model systems for HIV vaccine studies. Zwick *et al.* [2004] (**antibody interactions**)
- IgG1b12: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. IgG1b12 neutralized SOS and WT proteins comparably, and neither IgG1b12 nor the Fab b12 could neutralize well post-attachment, consistent with the notion that theb12 binding site would be blocked upon cellular binding. Binley *et al.* [2003] (**vaccine antigen design**)
- IgG1b12: Called 1b12. The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. CD4BS MAb IgG1b12 had no effect on B4e8 binding. Cavacini *et al.* [2003] (**antibody interactions**)
- IgG1b12: A sCD4-17b single chain chimera was made that can bind to the CD4 binding site, then bind and block co-receptor interaction. This chimeric protein is a very potent neutralizing agent, more potent than IgG1b12, 2G12 or 2F5 against Ba-L infection of CCR5-MAGI cells. It has potential for prophylaxis or therapy. Dey *et al.* [2003] (**immunoprophylaxis**, **immunotherapy**)
- IgG1b12: Four newborn macaques were challenged with pathogenic SHIV 89.6 and given post exposure prophylaxis using a combination of NAbs 2F5, 2G12, 4E10 and IgG1b12. 2/4 treated animals did not show signs of infection, and 2/4 macaques maintained normal CD4+ T cell counts and had a lower delayed peak viremia compared to the controls. Ferrantelli *et al.* [2003] (**antibody interactions**, **immunoprophylaxis**, **mother-to-infant transmission**)
- IgG1b12: Called b12 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution. Herrera *et al.* [2003] (**antibody interactions**)
- IgG1b12: MAbs IgG1b12, 2G12, 2F5 and 4E10 were tested for their ability to neutralize two primary HIV-1 clade A isolates (UG/92/031 and UG/92/037) and two primary HIV-1 clade D isolates (UG/92/001 and UG/92/005). 4E10 demonstrated the most potent cross-neutralization activity. Quadruple administration of MAbs IgG1b12, 2G12, 2F5, and 4E10 induced strong synergistic neutralization of 4 clade A isolates (UG/92/031, UG/92/037, RW/92/020 and RW/92/025) as well as 5 clade D isolates (UG/92/001,UG/9/005, /93/086/RUG/94/108, UG/94/114). The authors note this combination of 4 MAbs neutralizes primary HIV A, B, C, and D isolates. Kitabwalla *et al.* [2003] (**antibody interactions**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **mother-to-infant transmission**)
- IgG1b12: This review dicusses the importance and function of protective antibody responses in animal model studies in the context of effective vaccine development. SHIV models have shown protection using high levels of MAbs can prevent infection, and partial protection that can influence disease course can be obtained from modest levels of NAbs. SHIV challenges studies conducted with infusions of combinations of MAbs b12, 2G12, and 2F5 are reviewed. Mascola [2003] (**immunoprophylaxis**, **review**)

- IgG1b12: AC10 is a subject who was given treatment early after infection, and had a viral rebound after cessation of therapy, which then declined to a low level. The polyclonal sera from AC10 could potently neutralize the rebound virus, and NAb escape followed with a neutralizing response against the escape variant and subsequent escape from that response. Viral loads remained low in this subject despite escape. The rebound isolate that was potently neutralized by autologous sera was not particularly neutralization sensitive, as it resisted neutralization by sCD4 and MAbs IgG1b12, 2G12 and 2F5, and was only moderately sensitive to sera from other HIV+ individuals that had high titers of NAbs to TCLA strains. Montefiori *et al.* [2003] (**escape**)
- IgG1b12: Called b12 – Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 binding to those that affect binding of sCD4 and two non-neutralizing anti-CD4BS Abs b3 and b6 – while the epitope maps overlapped, there were some differences observed – binding of CD4 was never enhanced, indicating it had evolved to be optimal – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded – for twelve mutants, b12 neutralization sensitivity and affinity correlated, but for five mutants neutralization efficiency was maintained or increased despite a decrease in affinity suggesting that the subsitutions that influence b12 binding to the monomer are different than those that impact neutralization sensitivity to the trimer. Pantophlet *et al.* [2003a] (**antibody binding site definition and exposure**, **binding affinity**)
- IgG1b12: This paper describes an attempt to engineer a gp120 molecule that would focus the immune response onto the IgG1b12 epitope. Four Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with seven N-linked glycosylation site sequons and this combination minimized the binding of non-neutralizing MAbs. b12 affinity was lowered, and binding of non-neutralizing MAbs was knocked out. C1 and C5 regions were then removed to eliminate the epitopes for MAbs against these regions, but these also diminished IgG1b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- IgG1b12: Virion capture assays are not a good predictor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, but anti-V3 Abs 447-52D and 19b, which did not neutralize JR-CSF and ADA captured amounts of p24 equal to or higher than the amounts captured by the neutralizing Ab b12. Poignard *et al.* [2003] (**assay development**, **variant cross-recognition or cross-neutralization**)
- IgG1b12: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs F105, 15e, and IgG1b12 as well as their Fab fragments inhibited CD4-independent binding of the V1/V2 loop-deleted gp120 glycoproteins of R5 HIV-1 isolates ADA, YU2 and JR-FL and to CCR5 in a concentration dependent manner. CD4BS MAbs IgG1b12, F91 and F105 and their Fab counterparts (except for C11, used as a negative control) inhibited CD4-independent JR-FL and YU-2 gp120-CCR5 binding to CCR5-expressing Cf2Th cells and syncytium formation. Raja *et al.* [2003] (**co-receptor**)
- IgG1b12: Called b12. The NAb b12 was administered locally to the vagina in macaques and could protect against subsequent vaginal infection with SHIV-162P4. This NAb model of a topical microbicide was dose dependence, and was effective for up to 2 hours after administration. Veazey *et al.* [2003] (**immunoprophylaxis**, **mucosal immunity**)
- IgG1b12: Called b12. Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. Wang [2003] (**vaccine antigen design**, **review**)
- IgG1b12: Called b12. The Fab m18 was selected from a human phage display library by a new method called sequential antigen panning (SAP), using a series of antigens to screen the library to pick broadly cross-reactive isolates. The ability to block cell mediated fusion by m17 was compared to Fabs X5 and b12 for a clade A, CRF01 EA, G, and 6 clade B isolates, and the inhibitory activity of m18 was slightly lower but comparable to neutralizing Fabs b12 and X5. Zhang *et al.* [2003] (**inter-clade comparisons**)
- IgG1b12: The HIV-1 primary isolate DH012 has preserved the epitopes for the MAbs IgG1b12, 2G12, 17b, however natural DH012 infection in chimpanzees and DH012 gp120 vaccination in guinea pigs does not give rise to Abs against these epitopes. Zhu *et al.* [2003] (**vaccine-specific epitope characteristics**)
- IgG1b12: 4KG5, a single-chain Fv (scFv), reacts with a conformational epitope that is formed by the V1, V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Denaturation of gp120 abolished binding of 4KG5 and Fab b12. Addtionally, binding of 4KG5 was abrogated when any of the V1, V2 or V3 loops were deleted. Of a panel of Abs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished or abroated binding: V2 loop MAbs (G3-4, G3-136), V3 loop MAbs (19b, 447-52D, hNM01, AH48, loop2, F425 B4e8, 694-88D), V3-C4 (G3-299, G3-42, G3-519, G3-537), CD4BS (b6, b3, F91, F105, 15e, L33, 1008-D, 654-30D, 559-64D, 1027-30D, Ia3, Ia7, FG39, Fbb14). MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1, V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. 4KG5 did not enhance IgG1b12 neutralization. Zwick *et al.* [2003] (**antibody binding site definition and exposure**, **antibody interactions**)
- IgG1b12: IgG1b12 neutralized many South African (5/8) and Malawian (4/8) clade C primary HIV-1 isolates, being more effective than 2F5 which neutralized only two Malawian and no South African isolates. 2G12 did not neutralize any of the

16 isolates. Bures *et al.* [2002] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

- IgG1b12: This study examined Ab interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-gp41 MAb F240 enhanced the binding of CD4BS MAbs IgG1b12 and F105 to both R5X4 and R5 isolates, but had no effect on neutralization. Anti-V3 MAb B4a1 increased CD4BS MAbs IgG1b12 and F105 to R5X4 virions, but only IgG1b12 binding was increased by B4a1 to the R5 isolate, and neutralization was not impacted. Cavacini *et al.* [2002] (**co-receptor**)
- IgG1b12: A modified gp140 (gp140ΔCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. Chakrabarti *et al.* [2002] (**vaccine antigen design**)
- IgG1b12: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. Edwards *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- IgG1b12: Review of NAbs that notes IgG1b12 is a recombinant IgG1 from a phage displayed Fab generated against gp120 from a B clade infected individual, that it binds the CD4BS, that alone or in combination with other MAbs it can protect some macaques against SHIV infection, and that it has strong ADCC activity. Ferrantelli & Ruprecht [2002] (**review**)
- IgG1b12: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. Golding *et al.* [2002b]
- IgG1b12: HIV-1 gp160ΔCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160ΔCT with a reconstituted membrane ten-fold better than the same protein on beads—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160ΔCT PLs indistinguishably from gp160ΔCT expressed on the cell surface—non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12—the MAb 17b was sCD4 inducible on gp160ΔCT PL. Grundner *et al.* [2002] (**vaccine antigen design**)
- IgG1b12: A broad review of NAbs that mentions IgG1b12 as an example of a NAb that does not alter the conformation of gp120, but interferes with CD4 binding. Klasse & Sattentau [2002] (**review**)
- IgG1b12: Called b6. Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. Enthalpy and entropy changes were divergent, but compensated. CD4 and MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy of binding to the gp120 monomer (mean: 26.1 kcal/mol, range 18.6-31.5), but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. The high values suggest surface burial or protein folding and ordering of amino acids upon binding. NAb 2G12 had an entropy value of -1.6. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding that is not faced by other anti-gp120 antibodies. Kwong *et al.* [2002] (**antibody binding site definition and exposure**, **structure**)
- IgG1b12: Recombinant adeno-associated virus was used to deliver the IgG1b12 gene into mice by injection. IgG1b12 was expressed in these mice for over 6 months after the primary injection. This strategy allows for predetermined Ab specificity, and could ultimately be used with synergistic Ab combinations. Lewis *et al.* [2002] (**immunoprophylaxis**, **vaccine antigen design**)
- IgG1b12: A pseudotyping assay showed that an X4 V3 loop peptide could enhance infectivity of X4 virus, R5 and R5X4 V3 loops peptides could enhance infectivity of an R5 virus, and R5X4 peptides could enhance infectivity of an R5X4 virus. Neither R5 nor R5X4 peptides influenced binding of CD4BS MAbs F105 and Ig1Gb12, but did increase binding of CD4i MAb 17b. Ling *et al.* [2002] (**antibody binding site definition and exposure**, **co-receptor**)
- IgG1b12: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies. Liu *et al.* [2002] (**review**)
- IgG1b12: Deglycosylation of gp120 does not significantly affect IG1b12 binding, in contrast to MAB 2G12. Sanders *et al.* [2002] (**antibody binding site definition and exposure**)
- IgG1b12: The crystal structure of IgG1b12 is resolved and is the first structure of an intact human Ab with an ordered, full length hinge – the structure is extremely asymmetric and flexible with an antigen-binding site that has an unusually long CDR H3 region with a ten residue insertion that projects above the rest of the antigen-binding site – this loop may be required for recognition of the recessed CD4 binding site of gp120. Saphire *et al.* [2002] (**structure**)
- IgG1b12: Alanine scanning mutagenesis used in conjunction with competition and replacement studies of N-linked carbo-

hydrates and sugars suggest that the 2G12 epitope is formed from mannose residues contributed by the glycans attached to N295 and N332, with the other N-linked carbohydrates in positions N339, N386, and N392 playing a role in maintaining conformation relevant to 2G12 binding – N295A and N332A mutants showed essentially unchanged anti-CD4BS NAb b12 binding affinities, while N339A, N386A and N392A mutants displayed significantly lowered b12 affinity, presumably due to conformational changes. Scanlan *et al.* [2002] (**antibody binding site definition and exposure**)

- IgG1b12: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 – SOS gp140-2F5-IgG1b12 formed multiple ring structures composed of two SOS gp140 proteins bridged by two Ab molecules, while 2F5 and 2G12 formed extended chains rather than closed rings. Schulke *et al.* [2002] (**vaccine antigen design**)
- IgG1b12: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – Abs directed against the CD4 binding site (IgGCD4 and IgG1b12) reacted slightly more strongly with the gp120 monomer than with the oligomer, as did sCD4. Srivastava *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- IgG1b12: Called ARP3065: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. Vella *et al.* [2002] (**assay development**)
- IgG1b12: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b] (**antibody binding site definition and exposure**)
- IgG1b12: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. Xu *et al.* [2002] (**antibody interactions**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **mother-to-infant transmission**, **inter-clade comparisons**)
- IgG1b12: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140Δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002] (**vaccine antigen design**)
- IgG1b12: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: Called IgG1 b12. IgG1b12 induces strong ADCC and CDC cytoxicity of HIV-1 infected cells. A panel of mutants in the Fc region of IgG1b12 was generated. K322A reduced ADCC binding of FcγR and abolished complement-dependent cytotoxicity (CDC) and C1q binding. L234A plus L235 in the lower hinge region of the IgG1 heavy chain abolished both FcγR and C1q binding and ADCC and CDC. These mutants did not impact IgG1b12's ability to neutralize virus. Hezareh *et al.* [2001] (**ADCC**, **complement**)
- IgG1b12: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonates macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline – the most potent combination included IgG1b12, which alone does not alone neutralize SHIV89.6P. Hofmann-Lehmann *et al.* [2001] (**antibody interactions**, **immunoprophylaxis**)
- IgG1b12: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINC-NTS) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, except the mutation 197 S/R which resulted in a carbohydrate addition to 195 N that disrupts the IgG1b12 binding site. Kolchinsky *et al.* [2001] (**antibody binding site definition and exposure**)
- IgG1b12: Intravenous passive transfer of MAb b12 provides dose-dependent protection from infection to macaques vaginally challenged with the R5 virus SHIV(162P4) – the primary isolate HIV-1SF162 is neutralized 90% (IC90) by b12 at 2 μg/ml, and SHIV162P4, derived from HIV-1SF162, was neutralized by 90% at 2 μg/ml in PHA-activated PBMC from rhesus macaques – the 90% neutralization titers achieved in three groups of animals that were given 25-, 5-, and 1-mg/kg doses were approximately 1:400, 1:80, and 1:16, respectively –

the half-life of IgG1 b12 in plasma was about 1 week, but while the peak b12 plasma concentration was immediately after the infusion, the peak vaginal fluid concentration was 7-14 days later. Parren *et al.* [2001] (**immunoprophylaxis**, **kinetics**)

- IgG1b12: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – the structure of CD4-bound gp120 reveals features that HIV has evolved to escape anti-CD4BS Abs like IgG1b12 despite profound functional constraints – CD4BS Abs must first access the CD4 binding site, deeply recessed within the gp120 core, and the Fab of an Ab molecule is "wider" than CD4, and in addition the binding site is flanked by variable and glycosylated regions. Poignard *et al.* [2001] (**review**, **structure**)
- IgG1b12: This paper describes the technical aspects of the crystallization of b12 at a resolution of 2.7 angstroms with all 12 Ig domains resolved. Saphire *et al.* [2001a] (**structure**)
- IgG1b12: This paper describes the biological implications of the crystal structure of b12 – a remarkable feature of this antibody is a long protruding finger-like CDR H3 that can dock in the recessed CD4-binding site – a contact residues in gp120 are modeled, with numbering based on the variable loop-deleted crystal structure of gp120. Saphire *et al.* [2001b] (**structure**)
- IgG1b12: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. Si *et al.* [2001]
- IgG1b12: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12. Spenlehauer *et al.* [2001] (**assay development**)
- IgG1b12: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 M Abs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001] (**antibody interactions**, **co-receptor**)
- IgG1b12: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10. Xu *et al.* [2001] (**inter-clade comparisons**)
- IgG1b12: Primary isolates YU2 and ADA are more resistant to IgG1b12 neutralization than HXBc2: 90% Neutralization of HXBc2 is observed with 1.25 ug of IgG1b12, while ADA and YU2 require 2.5 and 5 ug respectively to achieve 50% neutralization, and 90% neutralization could not be achieved with 10 or 20 ug of IgG1b12, respectively. Yang *et al.* [2001] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. York *et al.* [2001] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three MAbs with respect to monomeric and oligomeric env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers. Zeder-Lutz *et al.* [2001] (**antibody interactions**)
- IgG1b12: b12 recognizes a conformational epitope that overlaps with the CD4 binding site – a phage displayed peptide library was used to identify a peptide which bound b12, called B2.1, which competes with b12 in competition assays – B2.1 has significant homology to the D loop of gp120: upper case letters indicate residues B2.1 shares with gp120, heRsymFS-DlenrcI – one of the goals of defining peptide mimics to the b12 epitope is to develop an immunogen that can stimulate b12-like antibodies, but B2.1 cross-linked to phage and ovalbumin bound IgG1b12 did not elicit cross-reactive gp120 Abs in mice or rabbits. Zwick *et al.* [2001a] (**antibody binding site definition and exposure**, **mimotopes**)
- IgG1b12: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – broadly neutralizing MAbs 2F5, IgG1b12, and 4E10 and Z13 fail to neutralize different subsets of viruses. Zwick *et al.* [2001b] (**inter-clade comparisons**)
- IgG1b12: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 – whole IgG1b12 and b12 Fab fragments behaved similarly in the neutralization assays – there was no evidence for cooperativity of binding between b12 and 2G12 to envelope spikes expressed on the cell surface of TCLA or primary isolates. Zwick *et al.* [2001c] (**antibody interactions**)

- IgG1b12: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. Grovit-Ferbas *et al.* [2000] (**vaccine antigen design**)
- IgG1b12: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not enhance neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows increased infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. Ly & Stamatatos [2000] (**escape**)
- IgG1b12: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12, binding to 22 of 26 isolates tested – 8 MAbs were tested for neutralization and MAb IgG1b12 was most potent, with 90% neutralization of 3/5 isolates tested. Nyambi *et al.* [2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- IgG1b12: Fab b12 was used – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000]
- IgG1b12: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – TCLA strains showed enhanced IgG1b12 neutralization sensitivity relative to PBMC-adapted lines – IgG1b12 was able to bind, with low affinity, to the rgp120 monomer HIV-1 W61D. Beddows *et al.* [1999] (**co-receptor**)
- IgG1b12: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999] (**vaccine antigen design**)
- IgG1b12: Neutralization assays with rsCD4, MAbs, and serum samples from SHIV-infected macaques and HIV-1 infected individuals were used to characterize the antigenic properties of the env glycoprotein of six primary isolate-like or TCLA SHIV variants. IgG1b12 neutralized SHIV strains HXBc2, KU2, 89.6, but not 89.6P and KB9. 89.6 is a dual tropic primary isolate that is not pathogenic in macaques, 89.6P is a highly pathogenic form of 89.6 obtained after passage in macaques, and KB9 is a molecular clone of 89.6P. Neutralization resistance was cell line independent. Crawford *et al.* [1999] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs. Hioe *et al.* [1999] (**antibody interactions**)
- IgG1b12: does not inhibit attachment of virus to cells and was used as a control of a study of neutralization by a MAb F58 based micro antibody. Jackson *et al.* [1999]
- IgG1b12: A meeting summary presented results regarding neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization *in vitro* corresponded to efficacy *in vivo*. Montefiori & Evans [1999] (**review**)
- IgG1b12: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – at day 6 post infection, mice were given 50 mg/kg of b12, an amount that would have been protective if given up to 8 hours post-infection, and 100-fold higher than the amount required for 90% neutralization *in vitro* – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs. Poignard *et al.* [1999] (**escape**, **immunotherapy**)
- IgG1b12: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type. Binley *et al.* [1998] (**antibody binding site definition and exposure**)
- IgG1b12: Immunoprecipitation of gp120 and gp160 expressed from a rec Semliki Forest virus by F105 and IgG1b12 indicated that the SFV expressed HIV-1 Env was folded appropriately – and SVF-HIV-1 Env vaccine gave the strongest anti-HIV-1 Env response in mice, when compared to an HIV-1 Env DNA vaccine and a rgp160 protein. Brand *et al.* [1998] (**vaccine antigen design**)

- IgG1b12: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D. Connor *et al.* [1998] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: Binds JRSF oligomer with high affinity, as do 205-46-9 and 2G6, but IgG1b12 is neutralizing, the other two are not – conclusions of this paper contrast with Parren98 – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect – rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2. Fouts *et al.* [1998] (**antibody binding site definition and exposure**)
- IgG1b12: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events. Frankel *et al.* [1998] (**antibody interactions**, **mucosal immunity**)
- IgG1b12: anti-C1 region MAb 87-135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) Kropelin *et al.* [1998] (**antibody interactions**)
- IgG1b12: Enhances binding of Hx10 to CD4 positive or negative HeLa cells, inhibits binding to CD4+ T-cell line A3.01 – neutralizes HeLa and A3.01 cell Hx10 infection. Mondor *et al.* [1998]
- IgG1b12: IgG1b12, Fab b12 and 3B3 derived from b12 were all included in this study – the rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope – binding affinity of divalent IgG1b12 is 17-fold greater than monovalent Fab b12. Parren *et al.* [1998a] (**binding affinity**)
- IgG1b12: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope. Parren *et al.* [1998b] (**variant cross-recognition or cross-neutralization**, **responses in children**)
- IgG1b12: MAbs 654-D100 and IgG1b12 neutralized viruses HIV-BRU and a mutated virus that lacks the V3 loop glycan equally effectively – in contrast, sera from guinea pigs immunized with BRU gp120 neutralize viruses more effectively that lack the V3 glycan. Schonning *et al.* [1998] (**antibody binding site definition and exposure**)
- IgG1b12: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2, but not V1, diminished neutralization by CD4BS MAb IgG1b12, in contrast to 654.30D and IgGCD4. Stamatatos & Cheng-Mayer [1998] (**vaccine antigen design**)
- IgG1b12: Fab b12 – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by subneutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment b12 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2. Sullivan *et al.* [1998a]
- IgG1b12: Induces Complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML. Takefman *et al.* [1998] (**complement**)
- IgG1b12: MAb was slightly more efficient at neutralization than Fab – inhibits viral binding to cells and viral entry – doesn't affect CD4-independent binding to T-cells. Valenzuela *et al.* [1998]
- IgG1b12: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding – IgG1b12 is an unusual CD4BS antibody because it is particularly potent as a neutralizing antibody and it is susceptible to changes in the V1-V2 stem loop structure, and so it may disrupt an interaction between CD4 and conserved amino acids on the V1-V2 stem. Wyatt *et al.* [1998] (**structure**)
- IgG1b12: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – IgG1b12 blocks CD4 binding and is the most potent neutralizing Ab – many 15 and 21-mer phage inserts were recognized, but it was not possible to derive a consensus – common features were a W and at least one acidic residue, and one sequence was found multiple times: NWPRWWEEFVDKHSS, and this peptide could compete with gp120 – two short stretches found in the phage peptides might mimic gp120 components of the epitope: positions 382-384, FFY(I), and 423-426 I(FV)I(V)NM. Boots *et al.* [1997] (**mimotopes**)
- IgG1b12: This is a review that includes a description of IgG1b12, noting approximately equivalent affinities for sgp120 and unprocessed gp160, and somewhat enhanced affinity for the native oligomer on TCLA viruses – primary viruses have reduced affinity, but still in the useful range for neutralization – there can be complete protection in hu-PBL-SCID mice with Ab even when administered several hours after viral challenge – competes with sCD4, but unlike other CD4BS antibodies, it is sensitive to mutations in V2. Burton & Montefiori [1997] (**review**)

- IgG1b12: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 mug per ml for 90% viral inhibition – IgG1b12 failed to neutralize only 1/9 primary isolates, although there was some variation between test sites. D'Souza *et al.* [1997] (**variant cross-recognition or cross-neutralization**, **assay standardization/improvement**)
- IgG1b12: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – IgG1b12 bound monomer, oligomer, and neutralized JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- IgG1b12: b12 was used in its IgG1 form – of 14 human MAbs, the most potent neutralizer of SHIV-vpu+, which expressed HIV-1 IIIB env – all Ab combinations tested showed synergistic neutralization – b12 has a synergistic response with MAbs 694/98-D (anti-V3), 2F5, and 2G12. Li *et al.* [1997] (**antibody interactions**)
- IgG1b12: JRCSF was cultured in the presence of IgG1b12 until a 100-fold resistance to neutralization was selected – resistance was due to three changes: V2 substitution D182N and C3 substitution P365L conferred resistance, and V2 D164N was also required for a viable virus – IgG1b12 resistant virus remained sensitive to MAbs 2G12 and 2F5. Mo *et al.* [1997] (**escape**)
- IgG1b12: Review: MAbs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes. Moore & Trkola [1997] (**review**)
- IgG1b12: Complete protection against HIV-1 infection was achieved in hu-PBL-SCID mice by passive immunization with physiologically relevant doses – pharmacokinetics showed serum half-life of 30.2 +/- 1.3 hours for Fab b12 and 7.4 +/- 0.7 days for IgG1 b12 in mice, but IgG1 half-lives in human are generally between 21-23 days. Parren *et al.* [1995]; Parren & Burton [1997] (**immunoprophylaxis**, **kinetics**)
- IgG1b12: In this review, the technique and potential application of Fab expression and selection in phage display libraries, and subsequent production of IgG molecules is discussed – b12 is exceptionally potent at neutralization and can successfully neutralize most B clade primary isolates, and many isolates from other subtypes as well – 3B3 was derived from b12 by selection for higher affinity using the CDR walking strategy – 3B3 has 8-fold enhancement of binding, a linear correlation was found between neutralization and affinity, and 3B3 can neutralize strains b12 cannot. Parren & Burton [1997] (**binding affinity**, **review**)
- IgG1b12: Fab b12 is unusual in that it binds to gp140 and monomeric gp120 with similar affinities, and with a higher affinity to the native oligomer—authors propose this antibody may be exceptional because it binds the virus rather than viral debris—IgG1b12 can protect against infection prior to or shortly after challenge of hu-PBL-SCID mice with TCLA strains and primary strains, but the serum concentrations required *in vivo* were higher than for *in vitro* neutralization. Parren *et al.* [1997b,a] (**antibody binding site definition and exposure**, **immunoprophylaxis**)
- IgG1b12: Inhibited some SI- and NSI-env chimeric viruses but enhanced one NSI-env chimeric virus 3 fold. Schutten *et al.* [1997] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- IgG1b12: Viral binding inhibition by IgG1b12 strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997]
- IgG1b12: Major deletions in C1 and C5 and deletions of the V1V2 and V3 loops do not diminish binding. Wyatt *et al.* [1997] (**antibody binding site definition and exposure**)
- IgG1b12: Saturation mutagenesis of the complementarity-determining region and optimization strategies were used to create very high affinity versions of this Fab – increased affinity was dominated by a slowing of the off rate. Yang *et al.* [1997c] (**binding affinity**)
- IgG1b12: 35 primary isolates were tested and all were neutralized by IgG1b12 (including 4, UG270, RW92/026, ZB20, and 301727 which been had reported as not neutralized by IgG1b12 Trkola *et al.* [1995]) – IgG1b12 could neutralize even when added after the virus to the culture – selection for 400-fold increased affinity did not enhance neutralization by antibody – IgG1b12 was more potent with greater breadth than MAb 2F5 Kessler II *et al.* [1997]. Kessler II *et al.* [1997]; Trkola *et al.* [1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- IgG1b12: Potent neutralizing *ex vivo* of virus taken directly from plasma of HIV-1 infected individuals – little correlation between neutralization sensitivity of passaged virus and plasma derived virus – more effective than MAb 19b. Gauduin *et al.* [1996] (**antibody interactions**)
- IgG1b12: Review: Unique among anti-CD4BS MAbs in terms of being potent against both lab adapted virus and primary isolates – one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates. Poignard *et al.* [1996b] (**review**)
- IgG1b12: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50-69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs. Poignard *et al.* [1996a] (**antibody interactions**)
- IgG1b12: Review: Only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5. Sattentau [1996] (**review**)
- IgG1b12: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a] (**antibody binding site definition and exposure**)
- IgG1b12: Because Fab b12 shows reduction in binding when the V2 loop is deleted and when aa 183/184 PI/SG substitutions are made competition studies were done with Fab L78 and anti-V2 MAbs SC258 and 684-238 and they do not compete with IgG1b12. Ditzel *et al.* [1995] (**antibody interactions**)
- IgG1b12: Called BM12 – broad cross-clade neutralization of primary isolates – additive neutralization in combination with MAb 2F5. Kessler *et al.* [1995] (**antibody interactions**, **inter-clade comparisons**)

- IgG1b12: Anti-CD4 binding site MAb – very potent neutralization of a number of primary isolates. Moore *et al.* [1995a] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: Review: unusual properties for anti-CD4 BS MAb: sensitive to V2 substitutions, preferential recognition of the oligomer on the cell surface. Moore & Ho [1995] (**review**)
- IgG1b12: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity. Sattentau *et al.* [1995] (**vaccine antigen design**)
- IgG1b12: Fab b12 showed potent neutralization of T-cell-line-adapted strains, but much reduced neutralization of 3 primary isolates – 2 of the 3 primary isolates also had reduced binding affinity, but the third was as efficiently immunoprecipitated as HXBc2. Sullivan *et al.* [1995] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: Could potently neutralize primary isolates from within clade B, but showed a slight reduction in efficacy outside of clade B. Trkola *et al.* [1995] (**inter-clade comparisons**)
- IgG1b12: Very potent neutralization, of primary and lab strains, at concentrations that could be achieved by passive immunization – reduced binding with A,C, and D clade viruses relative to B clade, poor reactivity with E clade – isolates that were refractive to neutralization by sera from HIV-1 + donors could be neutralized by IgG1 b12. Burton *et al.* [1994] (**inter-clade comparisons**)
- IgG1b12: Cross-reactive with some gp120s, (but not all), from clades A-D – not reactive with gp120 from clades E or F. Moore *et al.* [1994b] (**inter-clade comparisons**)
- IgG1b12: Anti-CD4 binding site Fab, potent neutralizing activity, greater affinity for a subpopulation of gp120 molecules suggested to be in a mature confirmation – mutations in gp120 that abrogate binding: 368 D/R or D/T, 370 E/R, and 477 D/V, of clone HXBc2 of LAI – sensitive to V1 and V2 substitutions. Roben *et al.* [1994] (**antibody binding site definition and exposure**)
- IgG1b12: The original Fab fragment was derived from a combinatorial phage library from bone marrow of an HIV-1 positive individual who had been asymptomatic for six years. Burton *et al.* [1991] (**antibody generation**)

No. 1046
MAb ID IgGCD4 (IgG-CD4)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype) human (IgG)
Ab Type CD4BS
References Srivastava *et al.* 2002; Ly & Stamatatos 2000; Stamatatos & Cheng-Mayer 1998; Capon *et al.* 1989

- IgGCD4: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – Abs directed against the CD4 binding site (IgGCD4 and IgG1b12) reacted slightly more strongly with the gp120 monomer than with the oligomer, as did sCD4. Srivastava *et al.* [2002]
- IgGCD4: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. Ly & Stamatatos [2000]
- IgGCD4: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 slightly enhanced neutralization by CD4BS MAb IgGCD4. Stamatatos & Cheng-Mayer [1998]
- IgGCD4: An antibody-like immunoadhesins molecule was constructed incorporating the gp120-binding domain of CD4. Capon *et al.* [1989]

No. 1047
MAb ID L28
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Ditzel *et al.* 1995
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review

- L28: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- L28: Substitutions at 257 T/R, 368 D/R, 370 E/R and 370 E/Q, 475 M/S 102 E/L and 463 N/D reduce binding – binding was enhanced by removal of the V3 loop and by substitutions 45 W/S, 298 R/G, 381 E/P, 382 F/L, 420 I/R, 435 Y/H or Y/R – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. Ditzel *et al.* [1995] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)

No. 1048
MAb ID L33
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Zwick *et al.* 2003; Ditzel *et al.* 1995

Keywords antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, review

- L33: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- L33: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- L33: binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. Ditzel *et al.* [1995] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)

No. 1049
MAb ID L41
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Ditzel *et al.* 1995
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review

- L41: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- L41: Substitutions at 133 D/R, 256 S/Y, 257 T/R, 368 D/R or D/T, 370 E/Q or E/R, 384 Y/E, and 421 K/L reduce binding – paradoxically, this Fab was retrieved from the library after masking with known anti-CD4BS MAbs – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. Ditzel *et al.* [1995] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)

No. 1050
MAb ID L42
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Ditzel *et al.* 1995
Keywords antibody binding site definition and exposure, review

- L42: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- L42: Substitutions at 257 T/R, 368 D/R, 370 E/R, 266 A/E and 477 D/V reduce binding – binding was significantly enhanced by 381 E/P and 382 F/L – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. Ditzel *et al.* [1995] (**antibody binding site definition and exposure**)

No. 1051
MAb ID L52
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Ditzel *et al.* 1995
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review

- L52: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- L52: Binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. Ditzel *et al.* [1995] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)

No. 1052
MAb ID L72
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype) mouse
Ab Type CD4BS
Research Contact Dr. Hariharam, IDEC Pharmaceuticals Corp La Jolla, CA
References Ditzel *et al.* 1997

- L72: Used to bind gp120 to solid phase to select MAbs from a phage selection library. Ditzel *et al.* [1997]

No. 1053
MAb ID M12
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS

Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- M12: There is a p15 gag specific MAb also named M12.
- M12: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M12 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – 50% neutralization of NL4-3 was achieved with 21 ug/ml of M12. Sugiura *et al.* [1999]
- M12: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1054
MAb ID M13
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- M13: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M13 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – 50% neutralization of NL4-3 was achieved with 35 ug/ml of M13. Sugiura *et al.* [1999]
- M13: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1055
MAb ID M6
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- M6: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M6 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. Sugiura *et al.* [1999]
- M6: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1056
MAb ID MAG 116
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type CD4BS
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 116: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L – neutralizes MN, IIIB and RF. Kang *et al.* [1994]

No. 1057
MAb ID MAG 12B
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type CD4BS
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 12B: Amino acid substitutions that reduce binding 10 fold: 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 477 D/V – weak neutralization of IIIB. Kang *et al.* [1994]

No. 1058
MAb ID MAG 29B
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type CD4BS
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 29B: Amino acid substitutions that reduce binding 10 fold: 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 386 N/Q, 421 K/L – weak neutralization of IIIB. Kang *et al.* [1994]

No. 1059
MAb ID MAG 3B
HXB2 Location Env
Author Location gp120
Epitope

Neutralizing no
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type CD4BS
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 3B: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R or A or G, 262 N/T, 368 D/R or T, 370 E/R or Q, 381 E/P, 384 Y/E, 421 K/L, 475 M/S, 477 D/V. Kang *et al.* [1994]

No. 1060
MAb ID MAG 55 (#55)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type CD4BS
Research Contact C. Y. Kang, IDEC Inc
References Moore & Sodroski 1996; Kang *et al.* 1994

- MAG 55: Called #55 – binding reciprocally inhibited by other anti-CD4 binding site MAbs, and by some C1-C5 MAbs – binding enhanced by anti-V3 MAb 110.5 and anti-V2 MAbs G3-136 and G3-4 – enhances binding of many anti-V3 and -V2 MAbs. Moore & Sodroski [1996]
- MAG 55: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 470 P/L, 475 M/S, 477 D/V – neutralizes MN, IIIB and RF. Kang *et al.* [1994]

No. 1061
MAb ID MAG 72 (L72)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type CD4BS
Research Contact C. Y. Kang or Dr. Hariharam, IDEC Pharmaceuticals Corp, La Jolla, CA
References Ditzel *et al.* 1997; Kang *et al.* 1994

- MAG 72: Called L72 – used to bind gp120 to solid phase to select MAbs from a phage selection library. Ditzel *et al.* [1997]
- MAG 72: Amino acid substitutions that reduce binding 10 fold: 257 T/R or A or G, 262 N/T, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 477 D/V – neutralizes MN, IIIB and RF. Kang *et al.* [1994]

No. 1062
MAb ID MAG 86
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type CD4BS
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 86: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 470 P/L, 477 D/V – neutralizes MN, IIIB and RF. Kang *et al.* [1994]

No. 1063
MAb ID MAG 96
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse
Ab Type CD4BS
Research Contact C. Y. Kang, IDEC Inc
References Kang *et al.* 1994

- MAG 96: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R – weak neutralization of IIIB. Kang *et al.* [1994]

No. 1064
MAb ID MTW61D
HXB2 Location Env
Author Location gp120 (W61D)
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Fouts *et al.* 1998; Sullivan *et al.* 1998a
Keywords enhancing activity, review

- MTW61D: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- MTW61D – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment MTW61D also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 – MTW61D was obtained by panning libraries derived from bone marrow from a long term asymptomatic donor against gp120 from primary isolate W61D. Sullivan *et al.* [1998a] (**enhancing activity**)

No. 1065
MAb ID S1-1
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Wisnewski *et al.* 1996; Moran *et al.* 1993; Lake *et al.* 1992
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, complement, enhancing activity, review

- S1-1: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- S1-1: S1-1 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. Wisnewski *et al.* [1996] (**antibody sequence, variable domain**)
- S1-1: Heavy (V HI) and light (V lambdaIII) chain sequenced – no enhancing activity – similar germline sequence to MAb 86, but very different activity. Moran *et al.* [1993] (**enhancing activity**, **antibody sequence, variable domain**)
- S1-1: Neutralizes IIIB and MN without complement, and neutralizes RF and a clinical isolate with complement – binds to native but not denatured gp120 – inhibits sCD4-gp120 binding. Lake *et al.* [1992] (**antibody binding site definition and exposure**, **complement**)

No. 1066
MAb ID T13
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- T13: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T13 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T13 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold. Sugiura *et al.* [1999]
- T13: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1067
MAb ID T49
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- T49: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T49 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T49 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold. Sugiura *et al.* [1999]
- T49: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1068
MAb ID T56
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type CD4BS
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- T56: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T56 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T56 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold. Sugiura *et al.* [1999]
- T56: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1069
MAb ID TH9
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen
Species (Isotype) human (IgG1κ)
Ab Type CD4BS
Research Contact Michael Fung, Tanox Biosystem, USA
References Gorny & Zolla-Pazner 2004; Yang *et al.* 1998; D'Souza *et al.* 1995
Keywords assay development, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- TH9: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)

- TH9: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. Yang *et al.* [1998] (**assay development**)
- TH9: Found to neutralize MN, but not JRCSF, two B subtype primary isolates, or a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs. D'Souza *et al.* [1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 1070
MAb ID anti-CD4BS summary
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
Ab Type CD4BS
References Moore & Sodroski 1996; Thali *et al.* 1993

- Anti-CD4 binding site antibodies (CD4BS) competitively inhibit CD4 binding to monomeric gp120, and they differ in precise dependence on gp120 residues, but generally require Asp-368 and Glu-370. Moore & Sodroski [1996]
- Shared components of MAb epitopes and the discontinuous CD4 binding regions included Thr 257, Asp 368, Glu 370, Lys 421 through Trp 427 and Asp 457. Thali *et al.* [1993]

No. 1071
MAb ID b11
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype) human
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Parren *et al.* 1998a
Keywords binding affinity, review

- b11: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- b11: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**binding affinity**)

No. 1072
MAb ID b13
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype) human
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Parren & Burton 1997; Parren *et al.* 1998a; Parren *et al.* 1995
Keywords binding affinity, immunoprophylaxis, review

- b13: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- b13: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**binding affinity**)
- b13: Fab b13 was used as a control in a hu-PBL SCID mouse study – animals were protected from HIV-1 SF2 infection by IgG1b12, somewhat by Fab b12, but not by b13. Parren *et al.* [1995]; Parren & Burton [1997] (**immunoprophylaxis**)

No. 1073
MAb ID b14
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype) human
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Parren *et al.* 1998a
Keywords binding affinity, review

- b14: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- b14: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**binding affinity**)

No. 1074
MAb ID b3
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing

Immunogen
Species (Isotype) human
Ab Type CD4BS
References Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Pantophlet *et al.* 2003a; Parren *et al.* 1998a; Parren *et al.* 1997b
Keywords antibody binding site definition and exposure, antibody interactions, binding affinity, review, vaccine antigen design, variant cross-recognition or cross-neutralization

- b3: This review summarizes MAbs directed to HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. Gorny & Zolla-Pazner [2004] (**review**)
- b3: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 binding to those that affect binding of sCD4 and two non-neutralizing anti-CD4BS Abs b3 and b6 – while the epitope maps overlapped, there were some differences observed – binding of CD4 was never enhanced, indicating it had evolved to be optimal – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded. Pantophlet *et al.* [2003a] (**antibody binding site definition and exposure**)
- b3: A gp120 molecule was design to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- b3: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)
- b3: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**binding affinity**)
- b3: Neutralizes TCLA strains, but not primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)

No. 1075
MAb ID b6
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen
Species (Isotype) human
Ab Type CD4BS
Research Contact Dennis Burton, Scripps, San Diego, CA, USA
References Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Pantophlet *et al.* 2003a; Poignard *et al.* 2003; Kwong *et al.* 2002; Parren *et al.* 1998a; Parren *et al.* 1997b
Keywords antibody binding site definition and exposure, antibody interactions, vaccine antigen design

- b6: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 binding to those that affect binding of sCD4 and two non-neutralizing anti-CD4BS Abs b3 and b6 – while the epitope maps overlapped, there were some differences observed – binding of CD4 was never enhanced, indicating it had evolved to be optimal – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded. Pantophlet *et al.* [2003a]
- b6: A gp120 molecule was design to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- b6: Virion capture assays are not a good predictor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – while b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, the Abs F105, 19b, and Fab b6 were overall very poor neutralizers. Poignard *et al.* [2003]
- b6: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected

by these loops. This was one of the CD4BS MAbs used. Zwick *et al.* [2003] (**antibody interactions**)

- b6: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- b6: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- b6: Neutralizes TCLA strains, but not primary isolates. Parren *et al.* [1997b]

No. 1076
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* CD4BS, Gag, V3
Species (Isotype) mouse
Ab Type CD4BS
References Truong *et al.* 1996

- Antibodies raised against recombinant anti-p55 virus-like particles with the p24 region 196-226 deleted, bearing inserts of either the V3 or the CD4BS regions of gp120 were studied – no neutralizing responses, weak Env and strong Gag responses were elicited – the major homology region (MHR) and proximal sequences was found to be required for capsid assembly. Truong *et al.* [1996]

No. 1077
MAb ID
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing yes
Immunogen
Species (Isotype) human
Ab Type CD4BS, CD4i, V2, V3
References Moore *et al.* 2001

- Moore and colleagues review structural aspects of gp120 and how they relate to antigenic domains, and review the data concerning the lack of a clear relationship between genetic subtype and serotype – they suggest the primary goal in vaccine efforts should be to design an immunogen that can be shown to elicit neutralizing antibodies against a significant proportion of primary isolates – assay artifacts that can result in confused interpretations are also discussed, such as Ab binding to defective spikes, which does not affect HIV-1 infectivity, but can dominant an assay signal. Moore *et al.* [2001]

No. 1078
MAb ID 17b (1.7b, sCD4-17b)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L P (wea
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4i
Research Contact James Robinson, Tulane University, New Orleans, LA, USA
References Pinter *et al.* 2004; Nabatov *et al.* 2004; McCaffrey *et al.* 2004; Ling *et al.* 2004; Liao *et al.* 2004; Biorn *et al.* 2004; Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Zhu *et al.* 2003; Ohagen *et al.* 2003; Xiang *et al.* 2003; Labrijn *et al.* 2003; Dey *et al.* 2003; Cavacini *et al.* 2003; Binley *et al.* 2003; He *et al.* 2003; Ling *et al.* 2002; Finnegan *et al.* 2002; Cavacini *et al.* 2002; Arthos *et al.* 2002; Zhang *et al.* 2002; Basmaciogullari *et al.* 2002; Grundner *et al.* 2002; Edwards *et al.* 2002; Xiang *et al.* 2002a; Xiang *et al.* 2002b; Dowd *et al.* 2002; Yang *et al.* 2002; Schulke *et al.* 2002; Golding *et al.* 2002b; Srivastava *et al.* 2002; Kwong *et al.* 2002; Finnegan *et al.* 2001; Poignard *et al.* 2001; Zhang *et al.* 2001a; York *et al.* 2001; Kolchinsky *et al.* 2001; Si *et al.* 2001; Rizzuto & Sodroski 2000; Yang *et al.* 2000; Stamatatos *et al.* 2000; Salzwedel *et al.* 2000; Park *et al.* 2000; Ly & Stamatatos 2000; Grovit-Ferbas *et al.* 2000; Binley *et al.* 1999; Hoffman *et al.* 1999; Oscherwitz *et al.* 1999a; Stamatatos & Cheng-Mayer 1998; Binley *et al.* 1998; Sullivan *et al.* 1998a; Sullivan *et al.* 1998b; Rizzuto *et al.* 1998; Moore & Binley 1998; Wyatt *et al.* 1998; Kwong *et al.* 1998; Parren *et al.* 1997b; Wyatt *et al.* 1997; Cao *et al.* 1997b; Ditzel *et al.* 1997; Weinberg *et al.* 1997; Li *et al.* 1997; Fouts *et al.* 1997; Binley *et al.* 1997a; Trkola *et al.* 1996a;

Wu *et al.* 1996; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; Wyatt *et al.* 1995; Beretta & Dalgleish 1994; Thali *et al.* 1994; Moore *et al.* 1993c; Thali *et al.* 1993

Keywords antibody binding site definition and exposure, co-receptor, vaccine antigen design, variant cross-recognition or cross-neutralization

- 17b: 48d and 17b have similar epitopes, and the pair are unique among human and rodent MAbs.
- 17b: NIH AIDS Research and Reference Reagent Program: 4091.
- 17b: The peptide 12p1 (RINNIPWSEAMM) inhibits direct binding of YU2 gp120 or Env trimer to CD4, CCR5 and MAb 17b in a concentration-dependent allosteric manner. 12p1 is thought to bind to unbound gp120 near the CD4 binding site, with a 1:1 stoichiometry. 12p1 also inhibited MAb F105 binding presumably because F105 favors an unactivated conformation, but not MAbs 2G12 or b12. The 1:1 stoichiometry, the fact that the peptide binding site is accessible on the trimer, the non-CD4 like aspect of the binding, and an ability to inhibit viral infection in cell cultures make it a promising lead for therapeutic design. Biorn *et al.* [2004]
- 17b: This review summarizes MAbs directed to HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. Gorny & Zolla-Pazner [2004]
- 17b: A32-rgp120 complexes opened up the CCR5 co-receptor binding site, but did not induce neutralizing antibodies with greater breadth among B subtype isolates than did uncomplexed rgp120 in vaccinated guinea pigs. 17b was used as a control to show A32-bound rgp120 had enhanced binding to this CD4-inducible MAb. Liao *et al.* [2004] (**vaccine antigen design**)
- 17b: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of 17b was decreased by trypsin, but increased by thrombin. Thrombin may increase HIV-induced cell fusion in blood by causing a conformational activating shift in gp120. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 17b: Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The loss of the glycan within the V3 loop (GM299 V3) and two sites adjacent to V3, C2 (GM292 C2) and (GM329 C3), increased neutralization susceptibility to CD4i FAb X5, but each of the glycan mutants and SF162 were refractive to neutralization with 48d and 17b. The loss of sites in C4 (GM438 C4), or V5 (GM454 V5) did not increase neutralization susceptibility to FAb X5. V3 glycans tended to shield V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans shielded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 17b: A set of HIV-1 chimeras that altered V3 net charge and glycosylation patterns in V1V2 and V3, involving inserting V1V2 loops from a late stage primary isolate taken after the R5 to X4 switch, were studied with regard to phenotype, co-receptor usage, and MAb neutralization. The loops were cloned into a HXB2 envelope with a LAI viral backbone. It was observed that the addition of the late-stage isolate V1V2 region and the loss of V3-linked glycosylation site in the context of high positive charge gave an X4 phenotype. R5X4, R5, and X4 viruses were generated, and sCD4, 2G12 and b12 neutralization resistance patterns were modified by addition of the late stage V1V2, glycosylation changes, and charge in concert, while neutralization by 2F5 was unaffected. 15e, 17b, and 48d could not neutralize any of the variants tested. Nabatov *et al.* [2004] (**antibody binding site definition and exposure**, **co-receptor**)
- 17b: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12 which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. Three CD4i MAbs were tested; all preferentially neutralized SF162, and JRFL became neutralization sensitive to CD4i Abs if the SF162 V1V2 loop was exchanged. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 17b: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. CD4i Abs 17b and X5 were weakly neutralizing in all formats, WT, SOS, and when added postbinding. Binley *et al.* [2003]
- 17b: Called 1.7b. The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. B4e8 enhanced binding of CD4i MAbs 4.8d, 1.7b, and A1g8 to R5X4 virus 92HT593, but only of 48d to the R5 virus 92US660, and there was only a modest impact of the combination of B4e8 and CD4i MAbs on neutralization. Cavacini *et al.* [2003]
- 17b: A sCD4-17b single chain chimera was made that can bind to the CD4 binding site, then bind and block co-receptor interaction. This chimeric protein is a very potent neutralizing agent, more potent than IgG1b12, 2G12 or 2F5 against Ba-L infection of CCR5-MAGI cells. It has potential for prophylaxis or therapy. It neutralized 5/6 R5 and X4 strains from the B clade, but was only moderately protective against a D clade isolate, and did not neutralize clade A, C, E, and F isolates. Dey *et al.* [2003]
- 17b: Vaccination of a gp120-CD4 fusion complex in six transgenic XMG2 XenoMouse mice that produce human IgG2 with K light chain did not produce any neutralizing antibodies. 36/39

MAbs derived from one of these mice were in one of two competition groups that were conformational and specific for the complex, suggesting this chimeric vaccine may be of little value, as immunodominant responses recognized epitopes not present in native Env. MAbs from the two CD4-gp120 complex-specific competition groups did not compete with MAbs with known targets on HIV-1 gp120, but their binding was enhanced by binding of 17b. He *et al.* [2003]

- 17b: This study shows the fragments of CD4i MAbs are better able to neutralize virus than whole IgG. Neutralization of HIV-1 R5 isolates JRFL, JR-CSF and ADA by CD4i MAbs X5, 17b, and 48d decreased with increased molecule size, the neutralizing potency of single-chain Fv (scFv) > than Fab fragments > whole Ab molecules. (With the exception of IgG 48d neutralization of HIV-1 ADA.) HIV-1 X4 isolates 89.6 and HxB2 are both relatively sensitive even to the larger IgG version. R5X4 isolate neutralization was dependent on the isolate and co-receptor usage. The CD4i MAb fragments neutralize HIV-1 subsequent to CD4 binding. The CD4i MAbs bind near the co-receptor binding sites on gp120. Co-receptors bind to the conserved beta19 strand and part of the V3 loop, regions that are masked by the V1V2 loops in the CD4-unbound state. When CD4 is bound, the co-receptor site is exposed near the membrane surface where it would be optimally accessible to co-receptors, and the smaller versions of the molecules are better able to overcome the steric hindrence. Labrijn *et al.* [2003]
- 17b: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. 17b recognized most variants,some from each of the four individuals, by gp120 immunoprecipitation. Ohagen *et al.* [2003]
- 17b: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b]
- 17b: This paper describes the generation of CD4i MAb E51, that like CD4i MAb 17b, blocks CCR5 binding to sCD4-bound gp120. E51 has more cross-neutralizing potency than other prototype CD4i MAbs (17b) for B and C clade isolates. E51 and 17b both neutralized HIV-1 clade B strains HXBc2 and ADA, while JR-FL and 89.6 were only neutralized by E51, not 17b. Clade C strains MCGP1.3 and SA32 were both inhibited by 17b and E51, but E51 was more potent against SA32. The substitutions E381R, F383S, R419D I420R, K421D, Q422L, I423S, and Y435S (HXB2 numbering) all severely reduce 17b and E51 binding. All but I423S also diminish CCR5 binding by more than 50%. The mutation F383S also inhibits sCD4 binding and F105 binding, and K421D inhibits F105 binding, but not sCD4. Xiang *et al.* [2003]
- 17b: The HIV-1 primary isolate DH012 has preserved the epitopes for the MAbs IgG1b12, 2G12, 17b, however natural DH012 infection in chimpanzees and DH012 gp120 vaccination in guinea pigs does not give rise to Abs against these epitopes. Zhu *et al.* [2003]
- 17b: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a CD4i MAb that had no impact on 4KG5 binding. Zwick *et al.* [2003]
- 17b: The two N-terminal domains of CD4, termed D1 and D2, when expressed in the absence of the remaining domains of CD4 retain the capacity to bind to gp120—coding sequences of D1D2 and Igαtp were fused to create a large, multivalent rec protein D1D2Igαtp, which, unlike CD4, does not enhance infection at sub-optimal concentrations—the MAb 17b can also enhance viral replication at sub-optimal concentrations, but D1D2-Igα inhibited the 17b enhancement of two primary isolates. Arthos *et al.* [2002]
- 17b: gp120 mutants were used to define the CXCR4 binding site using CXCR4 displayed on paramagnetic proteoliposomes (PMPLs) to reduce non-specific gp120 binding—basic residues in the V3 loop and the β19 strand (RIKQ, positions 419-422) were involved, and deletion of the V1-V2 loops allowed CD4-independent CXCR4 binding—MAbs 17b (CD4i) and F105 (CD4BS) were used to study conformational changes in the mutants—the affinity of ΔV1 and ΔV1-V2 for 17b was dramatically increased and no longer inducible in the presence of sCD4—V3 mutants R298A and R327A were not recognized by 17b except in the presence of sCD4—mutations in the β19 strand dramatically reduced 17b affinity in the presence or absence of sCD4, consistent with known 17b contact residues in this region. Basmaciogullari *et al.* [2002]
- 17b: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-V3 MAb B4a1 increased binding of CD4i MAbs 48d, 17b and A1g8, but only A1g8 binding was increased by B4a1 to the R5 isolate. Additive affects on neutralizaton of the R5X4 isolate with B4a1 and CD4i MAbs was observed, presumably due to increased exposure of the CD4i binding site, but not for the R5 isolate. Anti-gp41 MAb F240 had a synergistic effect on neutralization with CD4i MAbs 48d and 17b, but not with A1g8 for the R5X4 virus. Cavacini *et al.* [2002]
- 17b: CD4 residue Phe43 significantly contributes to the affinity of CD4-gp120 interactions – despite decreased affinities for gp120, CD4 proteins and CD4-mimetic peptides lacking a Phe side-chain enhance binding of gp120 to 17b in a manner similar to Phe-bearing ligands indicating the Phe42 interaction is not critical for CD4-induced conformational changes in gp120. Dowd *et al.* [2002]
- 17b: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent

MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. Edwards *et al.* [2002]

- 17b: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I and Cluster II MAbs required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor, binding to a fusion intermediate. 17b was used to demonstrate that the Cluster I and II MAbs bound to gp120/gp41 complexes, not to gp41 after shedding of gp120. Finnegan *et al.* [2002]
- 17b: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. Golding *et al.* [2002b]
- 17b: HIV-1 gp160ΔCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160ΔCT with a reconstituted membrane ten-fold better than the same protein on beads—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160ΔCT PLs indistinguishably from gp160ΔCT expressed on the cell surface—non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12—the MAb 17b was sCD4 inducible on gp160ΔCT PL. Grundner *et al.* [2002]
- 17b: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002]
- 17b: A pseudotyping assay showed that an X4 V3 loop peptide could enhance infectivity of X4 virus, R5 and R5X4 V3 loops peptides could enhance infectivity of an R5 virus, and R5X4 peptides could enhance infectivity of an R5X4 virus. Neither R5 nor R5X4 peptides influenced binding of CD4BS MAbs F105 and Ig1Gb12, but did increase binding of CD4i MAb 17b. Ling *et al.* [2002] (**antibody binding site definition and exposure**, **co-receptor**)
- 17b: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140. Schulke *et al.* [2002]
- 17b: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – 17b recognized both gp120 monomer and o-gp140. Srivastava *et al.* [2002]
- 17b: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b]
- 17b: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. Xiang *et al.* [2002a]
- 17b: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140Δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002]
- 17b: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization

sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002]

- 17b: Using a cell-fusion system, it was found CD4i antibodies 17b, 48d, and CG10 reacted faintly with Env expressing HeLA cells even in the absence of sCD4 or CD4 expressing target cells. Reactivity increased after sCD4 addition, but not after CD4 expressing target cell addition, and binding was not increased at the cell-to-cell CD4-Env interface. This suggests the CD4i co-receptor binding domain is largely blocked at the cell-fusion interface, and so CD4i antibodies would not be able access this site and neutralize cell-mediated viral entry. Finnegan *et al.* [2001]
- 17b: Mutations in two glycosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone—these same mutations tended to increase the neutralization sensitivity of the virus, including to 17b—only the CD4i antibodies 17b and 48d showed an increased affinity of the CD4 independent viruses relative to wild-type. Kolchinsky *et al.* [2001]
- 17b: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – the 17b epitope is masked prior to CD4 binding by the V1-V2 loop and in contrast to sCD4, the binding of cell surface CD4 to virus does not appear to make the epitope accessible to binding by 17b to allow neutralization. Poignard *et al.* [2001]
- SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. Si *et al.* [2001]
- 17b: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – 17b bound at somewhat greater levels to 168C than to 168P, but this is not a general feature of 17b binding to primary versus TCLA strains. York *et al.* [2001]
- 17b: 17b binds to a CD4 inducible epitope which partially overlaps the CCR5 binding site – JRFL, YU2, 89.6, and HXB2 and their C1-, V1/V2-, C5 -deletion mutants were used to study how 17b binding affects gp120-CD4 interactions – 17b reduced CD4-gp120 interactions by decreasing the on-rate and increasing the off-rate of sCD4, while enhanced binding of sCD4 binding was observed for the 17b-bound, V1/V2 deleted gp120s – 17b was considered to be a surrogate for CCR5, and the authors suggest that 17b binding may shift V1/V2 into a position that interferes with CD4 binding, forcing a release. Zhang *et al.* [2001a]
- 17b: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. Grovit-Ferbas *et al.* [2000]
- 17b: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. Ly & Stamatatos [2000]
- 17b: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000]
- 17b: Mutagenesis defines Ile-420, Lys-421, Gln-422, Pro-438, and Gly-441 to be important residues for CCR5 binding – these positions are located on two strands that connect the gp120 bridging sheet and outer domain, suggesting a mechanism for conformational shifts induced by CD4 binding to facilitate CCR5 binding. Rizzuto & Sodroski [2000]
- 17b: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – CD4i MAbs 17b and 48d have little effect on a standard cell fusion assay but potently block sCD4 activated fusion – 17b was broadly cross-reactive inhibiting sCD4 activated fusion with Env from clades A, B, C, D, E, F, and F/B. Salzwedel *et al.* [2000]
- 17b: Soluble gp140 derived from SF162, a neutralization-resistant primary isolate, and SF162AV2 a neutralization-susceptible isolate with 30 amino acids deleted from the V2 loop, were generated with or without the gp120-gp41 cleavage site intact – all forms are recognized by oligomer-specific MAb T4 and show enhanced binding of CD4i MAb 17b when sCD4 is bound – the fused forms are less efficiently recognized than the cleaved forms by polyclonal neutralizing sera from HIV-infected patients – the V3 loop is more exposed on the fused form. Stamatatos *et al.* [2000]
- 17b: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120

or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000]

- 17b: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999]
- 17b: A CD4-independent viral variant of IIIB, IIIBx, was generated on CXCR4-expressing cells – IIIBx exhibited greater exposure of the 17b and 48d epitopes and enhanced neutralization by CD4i MAbs and by polyclonal human sera – the 17b epitope has significant overlap with the CCR5 coreceptor binding site. Hoffman *et al.* [1999]
- 17b: A panel of MAbs was shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4i MAbs 17b and 48d bound better to the deleted protein than to wild type. Binley *et al.* [1998]
- 17b: 17b Fab was co-crystallized with a gp120 core and CD4, and it's binding site can be directly visualized—17b binds to the "bridging sheet" of gp120, an antiparallel beta sheet region, contacting residues from the C4 region and the V1/V2 stem—the contact area is small for an Ab-antigen interactive surface, and dominated in the Ab by the heavy chain—the center of the binding region has hydrophobic interactions, and the periphery charge interactions, acidic on 17b and basic on gp120. Kwong *et al.* [1998]
- 17b: Moore and Binley provide a commentary on the papers by Rizzuto *et al.* [1998], Wyatt *et al.* [1998] and Kwong *et al.* [1998] – they point out 17b shares binding elements in gp120 with chemokine receptor molecules, and that CD4 needs to bind to gp120 first to make the 17b epitope accessible and it may be sterically blocked in the CD4 bound virus, thus making it a poor NAb for primary isolates Moore & Binley [1998]. Kwong *et al.* [1998]; Moore & Binley [1998]; Rizzuto *et al.* [1998]; Wyatt *et al.* [1998]
- 17b: Site directed mutagenesis of a WU2 protein with the V1-V2 loops deleted revealed key residues for 17b-gp120 interaction and interaction of gp120 and CCR5 – mutations in residues that reduced 17b by 70% were R/D 419, I/R 420, Q/L 422, Y/S 435, I/S 423, K/D 121 and K/D 421– 17b can neutralize HIV-1 strains that use different chemokine receptors, supporting a common region in gp120 in chemokine-receptor interaction. Rizzuto *et al.* [1998]
- 17b: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 enabled neutralization by CD4i MAbs 17b and 48d. Stamatatos & Cheng-Mayer [1998]
- 17b: sCD4 induces 17b binding in primary isolates and TCLA strains – amino acids that reduce the efficiency of binding were determined and found also to compromise syncytia formation and viral entry – V1V2 deletion or sCD4 binding can expose the 17b epitope for both HXBc2 and macrophage tropic YU2 – neutralizing potency of 17b is probably weak due to poor exposure of the epitope – 17b epitope exposure upon sCD4 binding can occur over a wide range of temperatures, consistent with the energy of CD4 binding being sufficient to drive the V1/V2 loop into a new conformation. Sullivan *et al.* [1998b]
- 17b: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops, and the presence of V1/V2 increased the enhancement – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – 17b enhances YU2 enhanced viral entry 10-fold, whereas HXBc2 was neutralized. Sullivan *et al.* [1998a]
- 17b: Summary of the implications of the crystal structure of a gp120 core bound to CD4 and 17b, combined with what is known about mutations that reduce NAb binding to gp120 – probable mechanism of neutralization is interference with chemokine receptor binding – mutations in 88N, 117K, 121K, 256S, 257T, N262, Delta V3, E370, E381, F 382, R 419, I 420, K 421, Q 422, I 423, W 427, Y 435, P 438, M 475 of HXBc2 (IIIB) reduce binding – the only variable residues in gp120 that contact 17b are 202T and 434M – the contact points for 17b with the crystallized incomplete gp120 are mostly in the heavy chain of the Ab, and there is a gap between 17b's light chain and the partial gp120 which may be occupied by the V3 loop in a complete gp120 molecule – the authors propose that the V2 and V3 loops may mask the CD4i Ab binding site, and that the V2 loop may be repositioned upon CD4 binding. Wyatt *et al.* [1998]
- 17b: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to a CD4BS MAb, F105, or sCD4. Cao *et al.* [1997b]
- 17b: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 17b bound monomer, oligomer, and neutralized JRFL in the presence of sCD4, but if sCD4 was not present, 17b only bound monomer. Fouts *et al.* [1997]
- 17b: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 17b has synergistic response in combination with anti-V3 MAb 694/98-D. Li *et al.* [1997]

- 17b: Neutralizes TCLA strains, but not primary isolates. Parren *et al.* [1997b]
- 17b: 48d binds to the IIIB protein and not IIIB V3 peptide, while binding to the Can0A V3 peptide, suggesting Can0A V3 is a conformer that mimics the 48d – it does not bind to 17b, distinguishing the epitopes. Weinberg *et al.* [1997]
- 17b: Binds to sgp120 efficiently, but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – partial re-exposure if sCD4 was bound – could not bind to HXBc2 gp120 if the 19 C-term amino acids were deleted in conjunction with amino acids 31-93 in C1, but binding was restored in the presence of sCD4. Wyatt *et al.* [1997]
- 17b: Many MAbs inhibit binding (anti-C1, -C5, -C4, -CD4BS) – anti-V3 MAb 5G11 enhances binding, as do C1-C4 discontinuous epitopes A32 and 2/11c – enhances binding of some anti-V2 MAbs. Moore & Sodroski [1996]
- 17b: Binding did not result in significant gp120 dissociation from virion, in contrast to 48d, although the gp41 epitope of MAb 50-69 was exposed. Poignard *et al.* [1996a]
- 17b: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a]
- 17b: MIP-1α binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 — binding of 17b blocks this inhibition. Wu *et al.* [1996]
- 17b: Binds with higher affinity to monomer and oligomer, slow association rate, poor neutralization of lab strain – this is in contrast to 48d, which has very different kinetics. Sattentau & Moore [1995]
- 17b: Studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 17b in the presence sCD4 involves the V1/V2 loops, with more significant involvement of V2 – similar effect observed for 48d and A32. Wyatt *et al.* [1995]
- 17b: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 21h and 15e) Thali *et al.* [1994]
- 17b: Binding of 48d is much more influenced by sequence variation among molecular clones of LAI than is binding of 17b. Moore *et al.* [1993c]
- 17b: Epitope is better exposed upon CD4 binding to gp120 – competes with 15e and 21h, anti-CD4 binding site MAbs – 113 D/R, 252 R/W, 257 T/A or G, 370 E/D, 382 F/L, 420 I/R, 433A/L, 438 P/R and 475 M/S confer decreased sensitivity to neutralization. Thali *et al.* [1993]

No. 1079
MAb ID 21c
HXB2 Location Env
Author Location gp120 (IIIB, J62)
Epitope
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
Ab Type CD4i
Research Contact James Robinson, Tulane University, New Orleans, LA, USA
References Gorny & Zolla-Pazner 2004; Xiang *et al.* 2002b; Xiang *et al.* 2002a
Keywords antibody binding site definition and exposure, antibody generation, review, vaccine antigen design

- 21c: This review summarizes MAbs directed to HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 21c: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. Xiang *et al.* [2002a] (**antibody binding site definition and exposure**, **antibody generation**)
- 21c: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 1080
MAb ID 23e
HXB2 Location Env
Author Location gp120 (IIIB, J62)
Epitope
Subtype B
Neutralizing L
Immunogen HIV-1 infection
Species (Isotype) human (IgG)
Ab Type CD4i
Research Contact James Robinson, Tulane University, New Orleans, LA, USA
References Gorny & Zolla-Pazner 2004; Xiang *et al.* 2002b; Xiang *et al.* 2002a
Keywords antibody binding site definition and exposure, antibody generation, review, vaccine antigen design

- 23e: This review summarizes MAbs directed to HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 23e: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were

converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. Xiang *et al.* [2002a] (**antibody binding site definition and exposure**, **antibody generation**)

- 23e: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 1081
MAb ID 48d (4.8d, 4.8D)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L P (wea
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type CD4i
Research Contact James Robinson, Tulane University, New Orleans, LA, USA
References Pinter *et al.* 2004; Nabatov *et al.* 2004; McCaffrey *et al.* 2004; Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Labrijn *et al.* 2003; Cavacini *et al.* 2003; Cavacini *et al.* 2002; Zhang *et al.* 2002; Edwards *et al.* 2002; Xiang *et al.* 2002a; Xiang *et al.* 2002b; Yang *et al.* 2002; Golding *et al.* 2002b; Kwong *et al.* 2002; Finnegan *et al.* 2001; Verrier *et al.* 2001; Kolchinsky *et al.* 2001; Salzwedel *et al.* 2000; Yang *et al.* 2000; Park *et al.* 2000; Ly & Stamatatos 2000; Fortin *et al.* 2000; Hoffman *et al.* 1999; Oscherwitz *et al.* 1999a; Stamatatos & Cheng-Mayer 1998; Binley *et al.* 1998; Yang *et al.* 1998; Sullivan *et al.* 1998b; Parren *et al.* 1998a; Mondor *et al.* 1998; Wyatt *et al.* 1998; Frankel *et al.* 1998; Parren *et al.* 1997b; Wyatt *et al.* 1997; Ugolini *et al.* 1997; Lee *et al.* 1997; Weinberg *et al.* 1997; Li *et al.* 1997; Binley *et al.* 1997a; Trkola *et al.* 1996a; Poignard *et al.* 1996a; Moore & Sodroski 1996; Sattentau & Moore 1995; Sattentau *et al.* 1995; Wyatt *et al.* 1995; Sattentau 1995; D'Souza *et al.* 1995; Moore *et al.* 1994b; Thali *et al.* 1994; Moore *et al.* 1993c; Moore & Ho 1993; Thali *et al.* 1993
Keywords antibody binding site definition and exposure, antibody interactions, binding affinity, co-receptor, inter-clade comparisons, kinetics, review, structure, vaccine antigen design, variant cross-recognition or cross-neutralization

- 48d: 48d and 17b have similar epitopes, and the pair are unique among human and rodent MAbs.
- 48d: NIH AIDS Research and Reference Reagent Program: 1756.
- 48d: This review summarizes MAbs directed to HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 48d: Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The loss of the glycan within the V3 loop (GM299 V3) and two sites adjacent to V3, C2 (GM292 C2) and (GM329 C3), increased neutralization susceptibility to CD4i FAb X5, but each of the glycan mutants and SF162 were refractive to neutralization with 48d and 17b. The loss of sites in C4 (GM438 C4), or V5 (GM454 V5) did not increase neutralization susceptibility to FAb X5. V3 glycans tended to shield V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans shielded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 48d: A set of HIV-1 chimeras that altered V3 net charge and glycosylation patterns in V1V2 and V3, involving inserting V1V2 loops from a late stage primary isolate taken after the R5 to X4 switch, were studied with regard to phenotype, co-receptor usage, and MAb neutralization. The loops were cloned into a HXB2 envelope with a LAI viral backbone. It was observed that the addition of the late-stage isolate V1V2 region and the loss of V3-linked glycosylation site in the context of high positive charge gave an X4 phenotype. R5X4, R5, and X4 viruses were generated, and sCD4, 2G12 and b12 neutralization resistance patterns were modified by addition of the late stage V1V2, glycosylation changes, and charge in concert, while neutralization by 2F5 was unaffected. 15e, 17b, and 48d could not neutralize any of the variants tested. Nabatov *et al.* [2004] (**antibody binding site definition and exposure**, **co-receptor**)
- 48d: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. Three CD4i MAbs were tested; all preferentially neutralized SF162,

and JRFL became neutralization sensitive to CD4i Abs if the SF162 V1V2 loop was exchanged. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)

- 48d: Called 4.8d. The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. B4e8 enhanced binding of CD4i MAbs 4.8d, 1.7b, and A1g8 to R5X4 virus 92HT593, but only of 48d to the R5 virus 92US660, and there was only a modest impact of the combination of B4e8 and CD4i MAbs on neutralization. Cavacini *et al.* [2003] (**antibody interactions**, **co-receptor**)
- 48d: This study shows the fragments of CD4i MAbs are better able to neutralize virus than whole IgG. Neutralization of HIV-1 R5 isolates JRFL, JR-CSF and ADA by CD4i MAbs X5, 17b, and 48d decreased with increased molecule size, the neutralizing potency of single-chain Fv (scFv) > than Fab fragments > whole Ab molecules. (With the exception of IgG 48d neutralization of HIV-1 ADA being better than the Fab – for 48d, only the IgG and Fab forms were available, not the scFv.) HIV-1 X4 isolates 89.6 and HxB2 are both relatively sensitive even to the larger IgG version. R5X4 isolate neutralization was dependent on the isolate and co-receptor usage. The CD4i MAb fragments neutralize HIV-1 subsequent to CD4 binding. The CD4i MAbs bind near the co-receptor binding sites on gp120. Co-receptors bind to the conserved beta19 strand and part of the V3 loop, regions that are masked by the V1V2 loops in the CD4-unbound state. When CD4 is bound, the co-receptor site is exposed near the membrane surface where it would be optimally accessible to co-receptors, and the smaller versions of the molecules are better able to overcome the steric hindrence. Labrijn *et al.* [2003] (**antibody binding site definition and exposure**, **co-receptor**, **variant cross-recognition or cross-neutralization**)
- 48d: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- 48d: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a CD4i MAb that had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)
- 48d: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-V3 MAb B4a1 increased binding of CD4i MAbs 48d, 17b and A1g8, but only A1g8 binding was increased by B4a1 to the R5 isolate. Additive affects on neutralizaton of the R5X4 isolate with B4a1 and CD4i MAbs was observed, presumably due to increased exposure of the CD4i binding site, but not for the R5 isolate. Anti-gp41 MAb F240 had a synergistic effect on neutralization with CD4i MAbs 48d and 17b, but not with A1g8 for the R5X4 virus. Cavacini *et al.* [2002] (**variant cross-recognition or cross-neutralization**)
- 48d: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. Edwards *et al.* [2002] (**co-receptor**)
- 48d: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. Golding *et al.* [2002b]
- 48d: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- 48d: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.*

[2002b]

- 48d: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. Xiang *et al.* [2002a] (**antibody binding site definition and exposure**, **co-receptor**)
- 48d: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002]
- 48d: Called 4.8D – A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002] (**variant cross-recognition or cross-neutralization**)
- 48d: Using a cell-fusion system, it was found CD4i antibodies 17b, 48d, and CG10 reacted faintly with Env expressing HeLA cells even in the absence of sCD4 or CD4 expressing target cells. Reactivity increased after sCD4 addition, but not after CD4 expressing target cell addition, and binding was not increased at the cell-to-cell CD4-Env interface. This suggests the CD4i co-receptor binding domain is largely blocked at the cell-fusion interface, and so CD4i antibodies would not be able access this site and neutralize cell-mediated viral entry. Finnegan *et al.* [2001] (**antibody binding site definition and exposure**)
- 48d: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 48d – only the CD4i antibodies 17b and 48d showed an increased affinity of the CD4 independent viruses relative to wild-type. Kolchinsky *et al.* [2001]
- 48d: Called 4.8d – A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001]
- 48d: Called 4.8D – host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5beta or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab. Fortin *et al.* [2000]
- 48d: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. Ly & Stamatatos [2000]
- 48d: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. Park *et al.* [2000]
- 48d: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – CD4i MAbs 17b and 48d have little effect on a standard cell fusion assay but potently block sCD4 activated fusion. Salzwedel *et al.* [2000] (**co-receptor**)
- 48d: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. Yang *et al.* [2000]
- 48d: A CD4-independent viral variant of IIIB, IIIBx, was generated on CXCR4-expressing cells – IIIBx exhibited greater exposure of the 17b and 48d epitopes and enhanced neutralization by CD4i MAbs and by polyclonal human sera. Hoffman *et al.* [1999]
- 48d: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4i MAbs 17b and 48d bound better to the deleted protein than to wild type. Binley *et al.* [1998]
- 48d: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not

by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events. Frankel *et al.* [1998]
- 48d: Inhibits binding of Hx10 to both CD4 positive and CD4 negative HeLa cells. Mondor *et al.* [1998]
- 48d: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a]
- 48d: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 enabled neutralization by CD4i MAbs 17b and 48d. Stamatatos & Cheng-Mayer [1998]
- 48d: CD4i MAbs 17b and 48d compete with MAb CG10, and the binding sites may overlap – MAb A32 enhances binding of 17b, 48d and CG10. Sullivan *et al.* [1998b]
- 48d: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization of 48d is interference with chemokine receptor binding – CD4 binding increases exposure of epitope due to V2 loop movement – 88N, 117K, 121K, 256S, 257T, N262, delta V3, E370, E381, F 382, R 419, I 420, K 421, Q 422, I 423, W 427, Y 435, P 438, M 475 mutations in HXBc2 (IIIB) decrease binding. Wyatt *et al.* [1998] (**structure**)
- 48d: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. Yang *et al.* [1998]
- 48d: Prefers CD4-gp120 complex to gp120 alone, but does not enhance fusion, in contrast to MAb CG10, in fact it inhibits syncytium formation. Lee *et al.* [1997] (**antibody binding site definition and exposure**)
- 48d: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – all Ab combinations tested showed synergistic neutralization – 48d has synergistic response with MAbs 694/98-D (anti-V3) and F105. Li *et al.* [1997] (**antibody interactions**)
- 48d: Neutralizes TCLA strains, but not primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 48d: Viral binding inhibition by 48d was strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997]
- 48d: 48d binds to the IIIB protein and not IIIB V3 peptide, while binding to the Can0A V3 peptide, suggesting Can0A V3 is a conformer that mimics the 48d, (but not 17b), epitope. Weinberg *et al.* [1997] (**antibody binding site definition and exposure**)
- 48d: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding. Wyatt *et al.* [1997] (**antibody binding site definition and exposure**)
- 48d: Many MAbs inhibit binding (anti-C1, -C5, -C4, -CD4BS) – anti-C1-C4 discontinuous epitope MAbs A32 and 2/11c enhance binding – reciprocal enhanced binding with some anti-V2 MAbs. Moore & Sodroski [1996] (**antibody interactions**)
- 48d: Binding resulted in gp120 dissociation from virion, mimicking sCD4, and exposure of the gp41 epitope of MAb 50-69, in contrast to CD4BS MAbs. Poignard *et al.* [1996a] (**antibody interactions**)
- 48d: Neutralizes JR-FL – slightly inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a] (**antibody binding site definition and exposure**, **co-receptor**)
- 48d: Called 4.8D – Found to neutralize MN, but not JRCSF, two B subtype primary isolates, or a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs. D'Souza *et al.* [1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 48d: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity. Sattentau *et al.* [1995] (**vaccine antigen design**)
- 48d: Binds with similar affinity to monomer and oligomer, moderate association rate, potent neutralization – this is in contrast to 17b, which has very different kinetics. Sattentau & Moore [1995] (**antibody binding site definition and exposure**, **kinetics**, **binding affinity**)
- 48d: Studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 48d in the presence of sCD4 involves the V1/V2 loops, with more significant involvement of V2 – similar effect observed for 17b and A32. Wyatt *et al.* [1995] (**vaccine antigen design**)
- 48d: Poor cross-reactivity with gp120 from most clades. Moore *et al.* [1994b] (**inter-clade comparisons**)
- 48d: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 21h, 15e and 17b) Thali *et al.* [1994] (**variant cross-recognition or cross-neutralization**)
- 48d: Called 4.8d – Neutralizes IIIB – reactive with SF-2 gp120 – does not inhibit HIV-1 sera from binding to IIIB gp120. Moore & Ho [1993] (**variant cross-recognition or cross-neutralization**)
- 48d: Binding of 48d is much more influenced by sequence variation among molecular clones of LAI than is binding of 17b. Moore *et al.* [1993c] (**variant cross-recognition or cross-neutralization**)
- 48d: Epitope is better exposed upon CD4 binding to gp120 – competes with ICR 39.13, 15e and 21h, anti-CD4 binding site MAbs – inhibited by anti-CD4BS MAb ICR 39.13g and linear anti-C4 MAbs G3-42 and G3-508 – 113 D/R, 252 R/W, 257 T/A or G, 370 E/D, 382 F/L, 420 I/R, 421 K/L, 433A/L, 438 P/R and 475 M/S confer decreased sensitivity to neutralization. Thali *et al.* [1993] (**antibody binding site definition and exposure**, **antibody interactions**)

No. 1082
MAb ID 49e
HXB2 Location Env
Author Location gp120 (IIIB, J62)
Epitope
Subtype B
Neutralizing L
Immunogen HIV-1 infection

Species (Isotype) human (IgG)
Ab Type CD4i
Research Contact James Robinson, Tulane University, New Orleans, LA, USA
References Gorny & Zolla-Pazner 2004; Xiang *et al.* 2002b; Xiang *et al.* 2002a
Keywords antibody binding site definition and exposure, antibody generation, review, vaccine antigen design

- 49e: This review summarizes MAbs directed to HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 49e: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. Xiang *et al.* [2002a] (**antibody binding site definition and exposure**, **antibody generation**)
- 49e: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. Xiang *et al.* [2002b] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No. 1083
MAb ID Fbb21
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4i
References Zwick *et al.* 2003
Keywords antibody interactions

- Fbb21: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4i Fab first used in this study. Fbb21, like other CD4i MAbs, did not inhibit or enhance 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)

No. 1084
MAb ID Fbb21
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4i
References Zwick *et al.* 2003
Keywords antibody interactions

- Fbb21: scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4i Fab first used in this study. Fbb21, like other CD4i MAbs, did not inhibit or enhance 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)

No. 1085
MAb ID X5 (Fab X5)
HXB2 Location Env
Author Location gp120 (JRFL)
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type CD4i
References Pinter *et al.* 2004; McCaffrey *et al.* 2004; Darbha *et al.* 2004; Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2004; Zwick *et al.* 2003; Zhang *et al.* 2003; Labrijn *et al.* 2003; Binley *et al.* 2003; Moulard *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, co-receptor, inter-clade comparisons, review, structure, vaccine antigen design, variant cross-recognition or cross-neutralization

- X5: The structure of the Fab X5 was determined at 1.9 angstrom resolution. The binding site is a long, 22 amino acid CDR H3 with a hook shape. Long CDR H3s are also found in IgG1b12 (18 residues) and 17b (19 residues). FAb X5 has a W100, F100Y in the CDR H3 hook shown to be important for binding through site specific mutagenesis. Compared to JRCSF, Ala substitutions at eight residues reduced binding more than 3 fold: C119, K207, G367, M426, W427,

V430, I423, and K432. Only I423A and K432A were thought to possibly directly interact with X5, the other mutations were thought likely to disrupt the overall structure or CD4 binding. Darbha *et al.* [2004] (**antibody binding site definition and exposure**, **structure**)

- X5: This review summarizes MAbs directed to HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- X5: Sera from two HIV+ people and a panel of MAbs were used to explore susceptibility to neutralization in the presence or absence of glycans within or adjacent to the V3 loop and within the C2, C4 and V5 regions of HIV-1 SF162 env gp120. The loss of the glycan within the V3 loop (GM299 V3) and two sites adjacent to V3, C2 (GM292 C2) and (GM329 C3), increased neutralization susceptibility to CD4i FAb X5, but each of the glycan mutants and SF162 were refractive to neutralization with 48d and 17b. The loss of sites in C4 (GM438 C4), or V5 (GM454 V5) did not increase neutralization susceptibility to FAb X5. V3 glycans tended to shield V3 loop, CD4 and co-receptor MAb binding sites, while C4 and V5 glycans shielded V3 loop, CD4, gp41 but not co-receptor MAb binding sites. Selective removal of glycans from a vaccine candidate may enable greater access to neutralization susceptible epitopes. McCaffrey *et al.* [2004] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- X5: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. Three CD4i MAbs were tested; all preferentially neutralized SF162, and JRFL became neutralization sensitive to CD4i Abs if the SF162 V1V2 loop was exchanged. FAb X5 could neutralize both viruses, but had reduced potency against JRFL. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- X5: Called Fab X5. This paper is a study of the 2F5 NAb complexed to peptide ELDKWAS; the peptide was found to interact with amino acids near the base of the very long (22 residue) CDR 3H region of the Ab, although a Phe at the apex of the loop was also important. The authors suggest that particularly long CDR H3 regions may be a common feature of HIV-1 neuturalizing antibodies – there are 22 residues in 2F5's H3, 18 in b12's H3, and 22 residues in X5's H3. They express concern that because small animals like mice are unable to elicit Ab responses with such long H3s, they may be poor model systems for HIV vaccine studies. Zwick *et al.* [2004] (**antibody interactions**)
- X5: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. CD4i Abs X5 and 17b were weakly neutralizing in all formats, WT, SOS, and when added postbinding. Binley *et al.* [2003] (**vaccine antigen design**)
- X5: This study shows the fragments of CD4i MAbs are better able to neutralize virus than whole IgG. Neutralization of HIV-1 R5 isolates JRFL, JR-CSF and ADA by CD4i MAbs X5, 17b, and 48d decreased with increased molecule size, the neutralizing potency of single-chain Fv (scFv) > than Fab fragments > whole Ab molecules. (With the exception of IgG 48d neutralization of HIV-1 ADA.) HIV-1 X4 isolates 89.6 and HxB2 are both relatively sensitive even to the larger IgG version. R5X4 isolate neutralization was dependent on the isolate and co-receptor usage. The CD4i MAb fragments neutralize HIV-1 subsequent to CD4 binding. The CD4i MAbs bind near the co-receptor binding sites on gp120. Co-receptors bind to the conserved beta19 strand and part of the V3 loop, regions that are masked by the V1V2 loops in the CD4-unbound state. When CD4 is bound, the co-receptor site is exposed near the membrane surface where it would be optimally accessible to co-receptors, and the smaller versions of the molecules are better able to overcome the steric hindrence. Labrijn *et al.* [2003] (**antibody binding site definition and exposure**, **co-receptor**, **variant cross-recognition or cross-neutralization**)
- X5: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- X5: The Fab m18 was selected from a human phage display library by a new method called sequential antigen panning (SAP), using a series of antigens to screen the library to pick broadly cross-reactive isolates. The ability to block cell mediated fusion by m18 was compared to Fabs X5 and b12 for a clade A, CRF01 EA, G, and 6 clade B isolates, and the inhibitory activity of m18 was slightly lower but comparable to neutralizing Fabs b12 and X5. It also showed broad cross-neutralization; 11/15 pseudotyped Envs from primary isolates from clades A-F were inhibited in an IC50 assay at concentration less than or equal to 100 ug/ml; X5 was also tested and somewhat more potent, generally requiring lower concentrations and inhibiting 13/15 primary isolates. Zhang *et al.* [2003] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- X5: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a CD4i MAb that had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)
- X5: The human Fab X5 was selected from a phage display library derived from an HIV-1 positive donor with a highly neutralizing serum – it was selected for binding to purified

gp120-CD4-coreceptor complexes – the Fab neutralizes PBMC infection by a selection of HIV-1 primary isolates from clades A, B, C, D, E, F, and G, and neutralizes R5, X4, and R5X4 isolates – it binds to a conserved epitope on gp120 induced by CD4 binding, its binding is slightly enhanced by CCR5 binding – while CD4i MAb 17b binds the CCR5 binding site, X5 also competes with Fab b12 which overlaps with the CD4 binding site, suggesting the epitope for is near both the CD4 and CCR5 binding sites. Moulard *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 1086
MAb ID 8F101
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse (IgG)
Ab Type CD4i, gp120-CD4 complex
Research Contact Ranajiit Pal, Advanced BioScience Lab, Inc.
References Finnegan *et al.* 2002; Finnegan *et al.* 2001; DeVico *et al.* 1995
Keywords antibody binding site definition and exposure, antibody generation, kinetics

- 8F101: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I and Cluster II MAbs required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor, binding to a fusion intermediate. 8F101 selectively stains gp120-CD4 complexes after dissociation from gp41, and did not stain cells arrested earlier than 30 min of co-culture, but 8F101 and cluster I and II MAbs co-localized at fusing cell interfaces at 30 min coculture. After extended co-culture, only 8F101 bound. Finnegan *et al.* [2002] (**antibody binding site definition and exposure**, **kinetics**)
- 8F101: Using a cell-fusion system, it was found CD4i antibodies 17b, 48d, and CG10 reacted faintly with Env expressing HeLA cells even in the absence of sCD4 or CD4 expressing target cells. Reactivity increased after sCD4 addition, but not after CD4 expressing target cell addition, and binding was not increased at the cell-to-cell CD4-Env interface. This suggests the CD4i co-receptor binding domain is largely blocked at the cell-fusion interface, and so CD4i antibodies would not be able access this site and neutralize cell-mediated viral entry. However, CD4i MAbs 8F101 and A32, that bind outside the co-receptor domain, had a different pattern. They reacted after the formation of gp120-CD4-CXCR4 tri-complexes, so co-receptor interactions allowed exposure of their epitopes. Finnegan *et al.* [2001] (**antibody binding site definition and exposure**)
- 8F101: MAbs specifically reactive to crosslinked gp120 and CD4 were derived (8F101, 8F102) – conformation dependent – competition studies indicate the epitope is immunogenic in infected humans. DeVico *et al.* [1995] (**antibody generation**)

No. 1087
MAb ID T22
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type Env oligomer
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Otteken *et al.* 1996; Earl *et al.* 1994

- T22: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T22 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially blocked CD4 binding. Sugiura *et al.* [1999]
- T22: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp140 revealed that these anti-CD4BS MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes. Otteken *et al.* [1996]
- T22: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1088
MAb ID 2A2
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type N-term
References Weissenhorn *et al.* 1996

- Soluble gp41(21-166) forms a rod like structure that can be visualized with electron microscopy, and 2A2 binds to one end of the rod. Weissenhorn *et al.* [1996]

No. 1089
MAb ID AC4
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (Isotype) mouse
Ab Type N-term
References Dickey *et al.* 2000

- AC4: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) Dickey *et al.* [2000]

No. 1090
MAb ID AD3
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (Isotype) mouse
Ab Type N-term
References Cook *et al.* 1994; Dickey *et al.* 2000

- AD3: There may be two Abs with this name that bind to the N-term region of gp120. Cook *et al.* [1994]; Dickey *et al.* [2000]
- AD3: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) Dickey *et al.* [2000]

No. 1091
MAb ID AD3
HXB2 Location Env
Author Location gp120 (BH10)
Epitope
Neutralizing
Immunogen
Species (Isotype) mouse (IgG1)
Ab Type N-term
References Dickey *et al.* 2000; Cook *et al.* 1994; Ugen *et al.* 1993

- AD3: NIH AIDS Research and Reference Reagent Program: 2342.
- AD3: There may be two Abs with this name that bind to the N-term region of gp120. Cook *et al.* [1994]; Dickey *et al.* [2000]
- AD3: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. Cook *et al.* [1994]

No. 1092
MAb ID ID6
HXB2 Location Env
Author Location gp120 (1–193 BH10)
Epitope
Neutralizing
Immunogen
Species (Isotype) mouse (IgG1)
Ab Type N-term
References Dickey *et al.* 2000; Cook *et al.* 1994; Ugen *et al.* 1993

- ID6: NIH AIDS Research and Reference Reagent Program: 2343.
- ID6: There may be two Abs with this name that bind to the N-term region of gp120. Cook *et al.* [1994]; Dickey *et al.* [2000]
- ID6: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. Cook *et al.* [1994]

No. 1093
MAb ID ID6
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp160
Species (Isotype) mouse (IgG2a)
Ab Type N-term
References Cook *et al.* 1994; Dickey *et al.* 2000

- ID6: There may be two Abs with this name that bind to the N-term region of gp120. Cook *et al.* [1994]; Dickey *et al.* [2000]
- ID6: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) Dickey *et al.* [2000]

No. 1094
MAb ID 11/68b
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (HXB2)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10 *HIV component:* gp120
Species (Isotype) rat (IgG1)
Ab Type V1-V2
Research Contact Shotton and Dean
References Peet *et al.* 1998; Shotton *et al.* 1995; McKeating *et al.* 1993b

- 11/68b: 435 (Y/H) in C4 does not abrogate binding (John Moore, per comm, 1996)
- 11/68b: UK Medical Research Council AIDS reagent: ARP3041.
- 11/68b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/68b was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]
- 11/68b: Cross-competes with MAbs 62c, 66c, 66a, and CRA-4 – similar to MAb 62c – HXB2 neutralization escape mutant had a D/N substitution at residue 185 – non-reciprocal inhibition of binding of CRA-3 and CRA-6. Shotton *et al.* [1995]
- 11/68b: Changes at residues 183/184 (PI/SG) within V2, 435 (Y/H) in C4, abrogate binding. McKeating *et al.* [1993b]

No. 1095
MAb ID 62c
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG1)
Ab Type V1-V2
References Shotton *et al.* 1995

- 62c: UK Medical Research Council AIDS reagent: ARP3075.
- 62c: Cross-competes with MAbs 11/68b, 66c, 66a, and CRA-4 – same cross-competition group as MAb 11/68b – non-reciprocal inhibition of binding of CRA-3 and CRA-6 – substitutions 176-177 FY/AT, 179-180 LD/DL, 183-184 PI/SG, and 191-193 YSL/GSS abrogate binding – binds but does not neutralize Hx10. Shotton *et al.* [1995]

No. 1096
MAb ID CRA-6 (CRA6)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen
Species (Isotype) mouse
Ab Type V1-V2
References Shotton *et al.* 1995

- CRA-6: Called CRA6 – same competition group as CRA-3. Shotton *et al.* [1995]

No. 1097
MAb ID L15
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing P (weak)
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type V1-V2
References Gorny & Zolla-Pazner 2004; Parren *et al.* 1997b; Ditzel *et al.* 1997
Keywords review, variant cross-recognition or cross-neutralization

- L15: In a review of Envelope binding MAbs in this database, V2-specific MAbs are noted to have some ability to neutralize HIV-1, but generally weak with limited cross-reactivity. L15 and L17 are Fabs specific for V2. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- L15: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – 2 anti-V2 Fabs were obtained with very similar epitopes, L15 and L17 – deletions in V1 and V2 abolished binding, and rodent anti-V2 MAbs SC258, CRA3, G3-G4,G3-136, BAT-085, and 52-684 all compete with L15. Ditzel *et al.* [1997]
- L15: Does not neutralize TCLA strains but neutralizes some primary isolates weakly. Parren *et al.* [1997b]

No. 1098
MAb ID T52
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type V1-V2
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- T52: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T52 is one of two MAbs labeled B-II, that had limited cross-reactivity with seven clade B isolates and did not fully blocked CD4 binding – deletion of V1/V2 loops abrogated binding. Sugiura *et al.* [1999]
- T52: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1099
MAb ID T54
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type V1-V2
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- T54: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T54 is one of two MAbs labeled B-II, that had limited cross-reactivity with seven clade B isolates and did not fully blocked CD4 binding – deletion of V1/V2 loops abrogated binding. Sugiura *et al.* [1999]
- T54: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1100
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Neutralizing yes
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V1-V2 and V3-V5
References Gordon & Delwart 2000

- Primary isolates have great differences in susceptibility to neutralization – the variation in V1V2 and V3-V5 was measured by HTA in a set of viruses with a range of neutralization susceptibilities, and greater variability was uncorrelated with resistance to neutralization. Gordon & Delwart [2000]

No. 1101
MAb ID 1088
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
Ab Type V2
References Berman *et al.* 1997

- 1088: Binds weakly to 2/7 isolates from breakthrough cases from a MN gp120 vaccine trial. Berman *et al.* [1997]

No. 1102
MAb ID 110-B
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1
Species (Isotype) mouse
Ab Type V2
Research Contact Hybridolabs, Institute Pasteur, Paris, France
References Moore *et al.* 1993a

- 110-B: specific for BH10, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 168 K/L, 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS. Moore *et al.* [1993a]

No. 1103
MAb ID 1357
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype) human (IgG1κ)
Ab Type V2
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny & Zolla-Pazner 2004; Ling *et al.* 2002; Nyambi *et al.* 2000; Gorny *et al.* 2000; Nyambi *et al.* 1998
Keywords antibody binding site definition and exposure, co-receptor, review

- 1357: This broad review of anti-Envelope MAbs notes that V2 MAbs are generally weakly neutralizing at best, and somewhat strain specific. Anti-V2 MAbs 1357, 1361, 1393 are non-neutralizing. Gorny & Zolla-Pazner [2004] (**review**)
- 1357: A pseudotyping assay showed that an X4 V3 loop peptide could enhance infectivity of X4 virus, R5 and R5X4 V3 loops peptides could enhance infectivity of an R5 virus, and R5X4 peptides could enhance infectivity of an R5X4 virus. Neither R5 nor R5X4 peptides influenced binding of CD4BS MAbs F105 and Ig1Gb12, but did increase binding of CD4i MAb 17b. Of three V2 MAbs, only 830A, not 2158 or 1357 was enhanced by V3 peptide binding. Ling *et al.* [2002] (**antibody binding site definition and exposure**, **co-receptor**)
- 1357: Blocks binding of MAb 697-D to rgp120, and doesn't react with a protein from which V1V2 has been deleted – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold. Gorny *et al.* [2000]
- 1357: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. Nyambi *et al.* [2000]
- 1357: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. Nyambi *et al.* [2000]
- 1357: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind very weakly with a similar pattern of specificity to virions, but bound well to soluble gp120: weak binding only to subtype D MAL. Nyambi *et al.* [1998]

No. 1104
MAb ID 1361
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* gp120
Species (Isotype) human (IgG1κ)
Ab Type V2
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Nyambi *et al.* 2000; Gorny *et al.* 2000; Nyambi *et al.* 1998

- 1361: Blocks binding of MAb 697-D to rgp120, and doesn't react with a protein from which V1V2 has been deleted – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold. Gorny *et al.* [2000]
- 1361: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. Nyambi *et al.* [2000]

- 1361: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind weakly with a similar pattern of specificity to virions, but bound well to soluble gp120: weak binding to 1/4 B clade viruses (CA5), and also weak binding to a subtype D virus, MAL. Nyambi *et al.* [1998]

No. 1105
MAb ID 1393A
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype)
Ab Type V2
References Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000
Keywords inter-clade comparisons, review

- 1393A: This broad review of anti-Envelope MAbs notes that V2 MAbs are generally weakly neutralizing at best, and somewhat strain specific. Anti-V2 MAbs 1357, 1361, 1393A are non-neutralizing. Gorny & Zolla-Pazner [2004] (**review**)
- 1393A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. Nyambi *et al.* [2000] (**inter-clade comparisons**)

No. 1106
MAb ID 2158
HXB2 Location Env
Author Location gp120 (LAI)
Epitope
Subtype B
Neutralizing
Immunogen
Species (Isotype) human (IgG1κ)
Ab Type V2
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Pinter *et al.* 2004; Ling *et al.* 2004; Ling *et al.* 2002
Keywords antibody binding site definition and exposure, co-receptor, variant cross-recognition or cross-neutralization

- 2158: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of 17b and F105 was decreased by trypsin, but increased by thrombin. V2 MAbs 830A and 2158 were decreased by trypsin, uneffected by thrombin. Thrombin may increase HIV-induced cell fusion in blood by causing a conformational activating shift in gp120. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 2158: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. Three anti-V2 MAb were tested – both 2158 and 830A bound more strongly to JRFL, but neutralized SF162, and not neutralize JRFL. Thus V2 domains are better neutralization targets in SF162. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 2158: A pseudotyping assay showed that an X4 V3 loop peptide could enhance infectivity of X4 virus, R5 and R5X4 V3 loops peptides could enhance infectivity of an R5 virus, and R5X4 peptides could enhance infectivity of an R5X4 virus. Neither R5 nor R5X4 peptides influenced binding of CD4BS MAbs F105 and Ig1Gb12, but did increase binding of CD4i MAb 17b. Of three V2 MAbs, only 830A, not 2158 or 1357 was enhanced by V3 peptide binding. Ling *et al.* [2002] (**antibody binding site definition and exposure**, **co-receptor**)

No. 1107
MAb ID 66a
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (HXB2)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) mouse (IgG1)
Ab Type V2
References Shotton *et al.* 1995

- 66a: UK Medical Research Council AIDS reagent: ARP3074.
- 66a: Substitutions 176-177 FY/AT, 179-180 LD/DL, 183-184 PI/SG, and 191-193 YSL/GSS abrogate binding – same competition group as CRA4. Shotton *et al.* [1995]

No. 1108
MAb ID 66c
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (HXB2)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) mouse (IgG1)
Ab Type V2
References Shotton *et al.* 1995

- 66c: Substitutions 176-177 FY/AT, 179-180 LD/DL, 183-184 PI/SG, and 191-193 YSL/GSS abrogate binding – same competition group as CRA4. Shotton *et al.* [1995]

No. 1109
MAb ID 684-238 (52-684-238, 52-684)
HXB2 Location Env
Author Location gp120

Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp120
Species (Isotype) mouse
Ab Type V2
Research Contact Gerry Robey, Abbott Laboratories
References Ditzel *et al.* 1997; Moore & Sodroski 1996; Ditzel *et al.* 1995; Gorny *et al.* 1994; Thali *et al.* 1993; Moore *et al.* 1993a

- 684-238: Limited reciprocal enhancement of binding with anti-V3 and C4 region antibodies – reciprocal inhibition with V2 region antibodies. Moore & Sodroski [1996]
- 684-238: Does not compete with IgG1b12, reciprocal inhibition with MAbs L39, L40, and L78. Ditzel *et al.* [1995]
- 684-238: Weakly neutralizing, IC 50 = 84 mug/ml. Gorny *et al.* [1994]
- 684-238: Specific for BH10 or HXB2, does not bind to MN, RF, or SF-2 gp120 – neutralizes BH10 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177FY/AT, 179/180LD/DL, 183/184PI/SG, and 192-194YSL/GSS. Moore *et al.* [1993a]

No. 1110
MAb ID 830A
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype)
Ab Type V2
Research Contact Susan Zolla-Pazner
References Pinter *et al.* 2004; Ling *et al.* 2004; Gorny & Zolla-Pazner 2004; Ling *et al.* 2002; Nyambi *et al.* 2000
Keywords antibody binding site definition and exposure, co-receptor, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 830A: This broad review of anti-Envelope MAbs notes that V2 MAbs are generally weakly neutralizing at best, and somewhat strain specific. 830A neutralizes SF162. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 830A: The role of serine proteases on HIV infection was explored. Trypsin decreased the binding of most Env MAb tested and diminished cell fusion of H9 cells infected with HIV-1 LAI virus (H9/IIIB) to MAGI cells. In contrast, thrombin increased the binding of MAbs to gp120 epitopes near the CD4 and CCR5 binding sites, and increased cell fusion. Binding of 17b and F105 was decreased by trypsin, but increased by thrombin. V2 MAbs 830A and 2158 were decreased by trypsin, uneffected by thrombin. Thrombin may increase HIV-induced cell fusion in blood by causing a conformational activating shift in gp120. Ling *et al.* [2004] (**antibody binding site definition and exposure**)
- 2158: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. Three anti-V2 MAb were tested – both 2158 and 830A bound more strongly to JRFL, but neutralized SF162, and did not neutralize JRFL. Thus V2 domains are better neutralization targets in SF162. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 830A: A pseudotyping assay showed that an X4 V3 loop peptide could enhance infectivity of X4 virus, R5 and R5X4 V3 loops peptides could enhance infectivity of an R5 virus, and R5X4 peptides could enhance infectivity of an R5X4 virus. Neither R5 nor R5X4 peptides influenced binding of CD4BS MAbs F105 and Ig1Gb12, but did increase binding of CD4i MAb 17b. Of three V2 MAbs, only 830A, not 2158 or 1357 was enhanced by V3 peptide binding. Ling *et al.* [2002] (**antibody binding site definition and exposure**, **co-receptor**)
- 830A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. Nyambi *et al.* [2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 1111
MAb ID CRA-3 (CRA3)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) mouse (IgG2a)
Ab Type V2
Research Contact Mark Page, NIBSC AIDS reagent project, Potters Bar, Herts, UK
References Ditzel *et al.* 1997; Moore & Sodroski 1996; Shotton *et al.* 1995; Thali *et al.* 1993; Moore *et al.* 1993a; Moore & Ho 1993

- CRA-3: UK Medical Research Council AIDS reagent: ARP324.
- CRA-3: Many MAbs enhance binding, including some anti-C5, C1, V4, and C4 MAbs – enhances binding of only a small number of anti-V3 loop MAbs. Moore & Sodroski [1996]
- CRA-3: Called CRA3 – Same competition group as CRA6. Shotton *et al.* [1995]
- CRA-3: Conformational, does not bind well to denatured gp120. Moore & Ho [1993]
- CRA-3: specific for BH10 or HXB2, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT,

179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS – epitope probably involves stem of V1/V2 loop structure. Moore *et al.* [1993a]

No. 1112
MAb ID CRA-4 (CRA4)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (HXB2)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) mouse (IgG1)
Ab Type V2
Research Contact Mark Page, NIBS, MRC AIDS reagent repository, ARP 325
References Moore & Sodroski 1996; Shotton *et al.* 1995; Thali *et al.* 1993; Moore *et al.* 1993a; Moore & Ho 1993; McKeating *et al.* 1993b

- CRA-4: UK Medical Research Council AIDS reagent: ARP325.
- CRA-4: The only MAbs that enhanced binding were anti-V3 MAb 5G11 and anti-C1 MAb 135/9 binding – reciprocal inhibition of anti-V2 MAbs. Moore & Sodroski [1996]
- CRA-4: Cross-competes with MAbs 11/68b, 62c, 66c, 66a – similar to 66c and 66a – non-reciprocal inhibition by MAbs 12b, 60b and CRA-6. Shotton *et al.* [1995]
- CRA-4: Changes at residues 191/192/193 (YSL/GSS) within V2, 435 (Y/H) in C4, abrogate binding – type-specific neutralization. McKeating *et al.* [1993b]
- CRA-4: Conformational, does not bind well to denatured gp120. Moore & Ho [1993]
- CRA-4: Specific for BH10 and HXB2, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS. Moore *et al.* [1993a]

No. 1113
MAb ID L17
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype) human
Ab Type V2
References Gorny & Zolla-Pazner 2004; Kwong *et al.* 2002; Parren *et al.* 1998a; Ditzel *et al.* 1997
Keywords antibody binding site definition and exposure, binding affinity, review, variant cross-recognition or cross-neutralization

- L17: In a review of Envelope binding MAbs in this database, V2-specific MAbs are noted to have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L15 and L17 are Fabs specific for V2. Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **review**)
- L17: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- L17: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**binding affinity**)

No. 1114
MAb ID SC258 (52-581-SC258)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: gp120
Species (Isotype) mouse
Ab Type V2
Research Contact Gerry Robey, Abbott Laboratories
References He *et al.* 2002; Ditzel *et al.* 1997; Trkola *et al.* 1996a; Moore & Sodroski 1996; Ditzel *et al.* 1995; Moore *et al.* 1994b; Yoshiyama *et al.* 1994; Gorny *et al.* 1994; Thali *et al.* 1993; Moore *et al.* 1993a

- SC258: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. He *et al.* [2002]
- SC258: Several MAbs binding to various gp120 epitopes enhance binding, but the only MAb that SC258 enhanced binding of was anti-CD4 binding site MAb F91 – reciprocal inhibition with V2 region antibodies. Moore & Sodroski [1996]

- SC258: Does not inhibit gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study – listed as not neutralizing. Trkola *et al.* [1996a]
- SC258: Does not compete with IgG1b12 – reciprocal inhibition with MAbs L39, L40, and L78. Ditzel *et al.* [1995]
- SC258: Very poor reactivity with gp120 molecules outside of clade B. Moore *et al.* [1994b]
- SC258: HIV-1 RF V2 substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity – 177 Y/H inhibits SC258 neutralization. Yoshiyama *et al.* [1994]
- SC258: Called 52-581-SC258 – binds to BH10, MN, and RF gp120 – neutralizes BH10 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS. Moore *et al.* [1993a]

No. 1115
MAb ID L25
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (weak)
Immunogen HIV-1 infection
Species (Isotype) human (IgG1)
Ab Type V2-CD4BS
References Gorny & Zolla-Pazner 2004; Parren *et al.* 1997b; Ditzel *et al.* 1997; Ditzel *et al.* 1995
Keywords antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization

- L25: In a review of Envelope binding MAbs in this database, V2-specific MAbs are noted to have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L25, L39, L40 and L78 are Fabs specific for a complex binding site involving V2 and elements of the sCD4 binding site regions; among these only L25 and L78 mediate weak neutralization of some TCLA strains. Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **review**)
- L25: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – a single anti-V2-CD4 BS Fab was obtained with with sensitivity to substitutions in the V2 and CD4 BS regions – rodent anti-V2 MAb SC258 competes with L25. Ditzel *et al.* [1997]
- L25: Neutralizes TCLA strains weakly, but not primary isolates. Parren *et al.* [1997b]

No. 1116
MAb ID L39
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type V2-CD4BS
References Gorny & Zolla-Pazner 2004; Ditzel *et al.* 1995
Keywords antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization

- L39: In a review of Envelope binding MAbs in this database, V2-specific MAbs in are noted have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L25, L39, L40 and L78 are Fabs specific for a complex binding site involving V2 and elements of the sCD4 binding site regions; among these only L25 and L78 mediate weak neutralization of some TCLA strains. Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **review**)
- L39: This Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop (similar patterns were observed for L39 and L78 gp120 amino acid substitutions enhancing or reducing binding) – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – binding unaffected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684-238 – heavy and light chain variable region sequence is available. Ditzel *et al.* [1995]

No. 1117
MAb ID L40
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type V2-CD4BS
References Gorny & Zolla-Pazner 2004; Ditzel *et al.* 1995
Keywords antibody binding site definition and exposure, responses in children, variant cross-recognition or cross-neutralization

- L40: In a review of Envelope binding MAbs in this database, V2-specific MAbs are noted to have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L25, L39, L40 and L78 are Fabs specific for a complex binding site involving V2 and elements of the sCD4 binding site regions; among these only L25 and L78 mediate weak neutralization of some TCLA strains. Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **responses in children**)
- L40: This Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop (similar patterns were observed for L40 and L78 gp120 amino acid substitutions enhancing or reducing binding) – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – binding only partially affected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684-238 – heavy and light chain variable region sequence is available. Ditzel *et al.* [1995]

No. 1118
MAb ID L78
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L

Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type V2-CD4BS
References Gorny & Zolla-Pazner 2004; Kwong *et al.* 2002; Ditzel *et al.* 1995
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review, variant cross-recognition or cross-neutralization

- L78: In a review of Envelope binding MAbs in this database, V2-specific MAbs are noted to have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L25, L39, L40 and L78 are Fabs specific for V2 that are also associated with sCD4 binding site regions; among these only L25 and L78 mediate weak neutralization of some TCLA strains. Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **review**)
- L78: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- L78: Substitutions at V2: (152/153 GE/SM, 183/184 PI/SG, 191/193 YL/GS), 262 N/T, V3 (314 G/W), CD4BS (257 T/R, 368 D/R, 370 E/R) inhibit binding, and some C4 and C5 substitutions enhance binding – this Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – Fab neutralizes MN and LAI – binding unaffected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684-238 – heavy and light chain variable region sequence is available. Ditzel *et al.* [1995] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **antibody sequence, variable domain**)

No. 1119
MAb ID
HXB2 Location Env
Author Location gp120
Epitope
Subtype A, B, C
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
References Gilljam *et al.* 1999

- Sera from individuals with infections of HIV-1 subtype A-E were tested against purifed proteins from primary PBMC cultures. Sera reactivity tended not to be strongly related to subtype, rather probably reflected the sum of reactivities to conserved and variable regions in the proteins. V3 peptide comparisons showed some preference for within subtype binding. Gilljam *et al.* [1999]

No. 1120
MAb ID 10D8
HXB2 Location Env
Author Location gp160 (V3) (303–338)
Epitope
Subtype B
Neutralizing
Immunogen
Species (Isotype) human
Ab Type V3
References Callahan *et al.* 1991

- 10D8: Polyanionic polysaccharides were proposed to inhibit viral functions such as binding and syncytia formation through interations mediated through the local high positive charge density in the V3 loop. The binding of this anti-V3 antibody is inhibited by dextransulfate. Callahan *et al.* [1991]

No. 1121
MAb ID 10F6
HXB2 Location Env
Author Location gp160 (V3) (303–338)
Epitope
Subtype B
Neutralizing
Immunogen
Species (Isotype) human
Ab Type V3
References Callahan *et al.* 1991

- 10F6: Polyanionic polysaccharides were proposed to inhibit viral functions such as binding and syncytia formation through interations mediated through the local high positive charge density in the V3 loop. The binding of this anti-V3 antibody is inhibited by dextransulfate. Callahan *et al.* [1991]

No. 1122
MAb ID 110.J
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
Ab Type V3
Research Contact F. Traincard, Pasteur Institute, France
References Moore & Sodroski 1996; Thali *et al.* 1993

- 110.J: Binds to carboxy-terminal side of the V3 loop – reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – and reciprocal enhanced binding of some anti-V2 MAbs and anti-CD4 binding site MAbs. Moore & Sodroski [1996]
- 110.J: Inhibits sCD4-inducible anti-CD4 binding site MAb 48d. Thali *et al.* [1993]

No. 1123
MAb ID 11G5
HXB2 Location Env
Author Location gp160 (V3) (303–338)
Epitope
Subtype B
Neutralizing
Immunogen
Species (Isotype) human
Ab Type V3
References Callahan *et al.* 1991

- 11G5: Polyanionic polysaccharides were proposed to inhibit viral functions such as binding and syncytia formation through interations mediated through the local high positive charge density in the V3 loop. The binding of this anti-V3 antibody is inhibited by dextransulfate. Callahan *et al.* [1991]

No. 1124
MAb ID 2182
HXB2 Location Env
Author Location (JRCSF)
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Pinter *et al.* 2004; Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Gorny *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 2182: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary isolates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. Gorny & Zolla-Pazner [2004] (**review**, **inter-clade comparisons**)
- 2182: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using a JR-CSF fusion protein, and could neutralize 6/13 B clade viruses. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 2182: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. 5/6 anti-V3 MAbs had similar binding affinity to soluble SF162 and JR-FL rgp120s, although the V3 loop differs at three positions (HigpgrafyTtgE for JR-FL and TigpgrafyAtgD for SF162). Only the V3 MAb that had a different affinity was 2182, which bound to JRFL with higher affinity. Even 2182 preferentially neutralized SF162, however, the JRFL gp120 backbone with the SF162 V1V2 region was the more neutralization sensitive than pure SF162. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 2182: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2182 bound to 8/16 of the diverse isolates, not to any clade C or CRF01. Gorny *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 1125
MAb ID 2191
HXB2 Location Env
Author Location (JRCSF)
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3

Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Pinter *et al.* 2004; Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Gorny *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 2191: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary isolates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**)
- 2191: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using a JR-CSF fusion protein, and could neutralize 8/13 B clade viruses. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 2191: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. 5/6 anti-V3 MAbs, including 2191, had similar binding affinity to soluble SF162 and JR-FL rgp120s, although the V3 loop differs at three positions (HigpgrafyTtgE for JR-FL and TigpgrafyAtgD for SF162). Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 2191: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2191 bound to 10/16 of the diverse isolates, not to any clade D or CRF01. Gorny *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 1126
MAb ID 2219
HXB2 Location Env
Author Location (JRCSF)
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Pinter *et al.* 2004; Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Gorny *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 2219: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary isolates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**)
- 2219: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using a JR-CSF fusion protein, and could neutralize 6/13 B clade viruses. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 2219: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12,

which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. 5/6 anti-V3 MAbs, including 2219, had similar binding affinity to soluble SF162 and JR-FL rgp120s, although the V3 loop differs at three positions (HigpgrafyTtgE for JR-FL and TigpgrafyAtgD for SF162). Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)

- 2219: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2219 bound to 13/16 of the diverse isolates. Gorny *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 1127
MAb ID 2412
HXB2 Location Env
Author Location gp120 (V3) (JRCSF)
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Gorny *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization

- 2412: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary isolates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. Gorny & Zolla-Pazner [2004] (**antibody binding site definition and exposure**, **review**)
- 2412: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using a JR-CSF fusion protein, and could neutralize 4/13 B clade viruses. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 2412: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2412 bound to 7/16 of the diverse isolates, and did not bind to any of the clade C, D or CRF01 viruses. Gorny *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No. 1128
MAb ID 2442
HXB2 Location Env
Author Location (JRCSF)
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)

References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Gorny *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization

- 2442: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary isolates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 2442: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using a JR-CSF fusion protein, and could neutralize 9/13 B clade viruses. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 2442: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2442 bound to 13/16 of the diverse isolates. Gorny *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **review**)

No. 1129
MAb ID 2456
HXB2 Location Env
Author Location (JRCSF)
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Gorny *et al.* 2002
Keywords antibody binding site definition and exposure, review

- 2456: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary isolates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. Gorny & Zolla-Pazner [2004] (**review**)
- 2456: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using a JR-CSF fusion protein, and could neutralize 4/12 B clade viruses. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 2456: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2456 bound to 12/16 of the diverse isolates. Gorny *et al.* [2002]

No. 1130
MAb ID 2483
HXB2 Location Env

Author Location Env (JR-CSF)
Epitope
Subtype B
Neutralizing P
Immunogen
Species (Isotype) human
Ab Type V3
Research Contact Dr. Zolla-Pazner, Veterans Affairs Center, NY, NY. zollas01@endeavor.med.nyu.edu
References Gorny *et al.* 2004
Keywords antibody binding site definition and exposure

- 2483: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This antibody was selected using a JRCSF fusion protein. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)

No. 1131
MAb ID 2497
HXB2 Location Env
Author Location Env (JR-CSF)
Epitope
Subtype B
Neutralizing P
Immunogen
Species (Isotype) human
Ab Type V3
Research Contact Dr. Zolla-Pazner, Veterans Affairs Center, NY, NY. zollas01@endeavor.med.nyu.edu
References Gorny *et al.* 2004
Keywords antibody binding site definition and exposure

- 2497: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This antibody was selected using a JRCSF fusion protein. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)

No. 1132
MAb ID 2557
HXB2 Location Env
Author Location Env (JR-CSF)
Epitope
Subtype B
Neutralizing P
Immunogen
Species (Isotype) human
Ab Type V3
Research Contact Dr. Zolla-Pazner, Veterans Affairs Center, NY, NY. zollas01@endeavor.med.nyu.edu
References Gorny *et al.* 2004
Keywords antibody binding site definition and exposure

- 2557: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This antibody was selected using a JRCSF fusion protein. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)

No. 1133
MAb ID 2558
HXB2 Location Env
Author Location Env (92UG037)
Epitope
Subtype A
Neutralizing P
Immunogen
Species (Isotype) human
Ab Type V3
Research Contact Dr. Zolla-Pazner, Veterans Affairs Center, NY, NY. zollas01@endeavor.med.nyu.edu
References Gorny *et al.* 2004
Country Uganda
Keywords antibody binding site definition and exposure

- 2558: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This antibody was selected using an A clade fusion protein, 92UG037. It is unusual in that it is a V3 antibody selected for conformational aspects using an A clade virus, with a V3 GPGQ tip – clade B viruses are usually used and have GPGR tips. It cross-neutralizes and binds B clade HIV SF162. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)

No. 1134
MAb ID 2580
HXB2 Location Env
Author Location Env (JR-CSF)
Epitope
Subtype B
Neutralizing P
Immunogen
Species (Isotype) human
Ab Type V3
Research Contact Dr. Zolla-Pazner, Veterans Affairs Center, NY, NY. zollas01@endeavor.med.nyu.edu
References Gorny *et al.* 2004
Keywords antibody binding site definition and exposure

- 2580: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This antibody was selected using a JRCSF fusion protein. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)

No. 1135
MAb ID 391/95-D
HXB2 Location Env
Author Location Env
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
Research Contact S. Zolla-Pasner
References Guillon *et al.* 2002a
Keywords co-receptor, enhancing activity

- 391/95-D: This antibody was used to explore the sensitivity of chimeric envelope viruses to Ab-mediated enhancement or neutralization. V3 mediated enhancement and envelopes susceptible to enhancement used CCR5. Enhancement was CD4 dependent. Guillon *et al.* [2002a] (**co-receptor**, **enhancing activity**)

No. 1136
MAb ID 39F
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing no
Immunogen
Species (Isotype)
Ab Type V3
Research Contact James Robinson, Tulane University, New Orleans, LA, USA
References Kwong *et al.* 2002; Grundner *et al.* 2002; Yang *et al.* 2002
Keywords antibody binding site definition and exposure

- 39F: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface. Grundner *et al.* [2002]
- 39F: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- 39F: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002]

No. 1137
MAb ID 4148d
HXB2 Location Env
Author Location Env
Epitope
Subtype B
Neutralizing
Immunogen
Species (Isotype)
Ab Type V3
Research Contact Abraham Pinter, Public Health Research Institute, Newark, NJ, 07103. pinter@phri.org
References Pinter *et al.* 2004; Pinter *et al.* 1993b
Keywords antibody generation, variant cross-recognition or cross-neutralization

- 4148D: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. 5/6 anti-V3 MAbs, including 4148D, had similar binding affinity to soluble SF162 and JR-FL rgp120s, although the V3 loop differs at three positions (HigpgrafyTtgE for JR-FL and TigpgrafyAtgD for SF162). Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 4148D: Pinter1993a first describes this MAb. Pinter *et al.* [1993b] (**antibody generation**)

No. 1138
MAb ID 55/68b
HXB2 Location Env
Author Location gp120 (300–315)
Epitope
Neutralizing
Immunogen
Species (Isotype)
Ab Type V3
References Peet *et al.* 1998

- 55/68b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/68b binding was abrogated by V3 serine substitutions in the V3 loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]

No. 1139
MAb ID 5G11
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
Ab Type V3
Research Contact S. Nigida and L. Arthur, NCI, Frederick, MD USA
References Moore & Sodroski 1996

- 5G11: Binds to conformation sensitive epitope in the V3 loop – reciprocal inhibition of other V3 loop MAbs – reciprocal enhancement of some C1-C5 MAbs (unusual for an anti-V3 MAb) and CD4 binding site MAbs – and enhances binding of V2 MAbs. Moore & Sodroski [1996]

No. 1140
MAb ID 6.1
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V3
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords review

- 6.1: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. 6.1 was non-neutralizing. Gorny & Zolla-Pazner [2004] (**review**)
- 6.1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 3/4 V3 MAbs bound a similar linear epitope between positions 11-30 of the MN V3 loop (8E11/A8, 6.1, and 6.7), but only 8E11/A8 could weakly neutralize autologous strain SF162. He *et al.* [2002]

No. 1141
MAb ID 6.7
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V3
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, review

- 6.7: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. 6.7 was non-neutralizing. Gorny & Zolla-Pazner [2004] (**review**)
- 6.7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 3/4 V3 MAbs bound a similar linear epitope between positions 11-30 of the MN V3 loop (8E11/A8, 6.1, and 6.7), but only 8E11/A8 could weakly neutralize autologous strain SF162. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**)

No. 1142
MAb ID 8.27.3
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V3
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords review, variant cross-recognition or cross-neutralization

- 8.27.3: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, like 8.27.3; a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 8.27.3: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 1/4 V3 MAbs, 8.27.3, bound a discontinuous epitope that was broadly cross-reactive with B clade R5 and X4 strains

(not E clade) and could neutralize autologous strain SF162. He *et al.* [2002]

No. 1143
MAb ID 8E11/A8
HXB2 Location Env
Author Location gp120 (SF162)
Epitope
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Species (Isotype) transgenic mouse (IgG2κ)
Ab Type V3
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny & Zolla-Pazner 2004; He *et al.* 2002
Keywords antibody binding site definition and exposure, antibody generation, autologous responses, review

- 8E11/A8: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 8E11/A8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 3/4 V3 MAbs bound a similar linear epitope between positions 11-30 of the MN V3 loop (8E11/A8, 6.1, and 6.7), but only 8E11/A8 could weakly neutralize autologous strain SF162. He *et al.* [2002] (**antibody binding site definition and exposure**, **antibody generation**, **autologous responses**)

No. 1144
MAb ID 9305
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen
Species (Isotype) mouse
Ab Type V3
Research Contact Du Pont, Wilmington DE
References McDougal *et al.* 1996

No. 1145
MAb ID A1g8
HXB2 Location Env
Author Location gp120
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact James Robinson, Tulane University Med School, New Orleans, LA, USA
References Cavacini *et al.* 2003; Cavacini *et al.* 2002
Keywords antibody interactions, co-receptor, variant cross-recognition or cross-neutralization

- A1g8: The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. B4e8 enhanced binding of CD4i MAbs 4.8d, 1.7b, and A1g8 to R5X4 virus 92HT593, but only of 48d to the R5 virus 92US660, and there was only a modest impact of the combination of B4e8 and CD4i MAbs on neutralization. Cavacini *et al.* [2003] (**antibody interactions**, **co-receptor**)
- A1g8: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-V3 MAb B4a1 increased binding of CD4i MAbs 48d, 17b and A1g8, but only A1g8 binding was increased by B4a1 to the R5 isolate. Additive affects on neutralizaton of the R5X4 isolate with B4a1 and CD4i MAbs was observed, presumably due to increased exposure of the CD4i binding site, but not for the R5 isolate. Anti-gp41 MAb F240 had a synergistic effect on neutralization with CD4i MAbs 48d and 17b, but not with A1g8 for the R5X4 virus. Cavacini *et al.* [2002] (**antibody interactions**, **co-receptor**, **variant cross-recognition or cross-neutralization**)

No. 1146
MAb ID AG1121 (1121)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen
Species (Isotype)
Ab Type V3
Research Contact AGMED, Inc, Bedford, MA, USA or ImmunoDiagnostics, Inc, Woburn, MA, USA
References Si *et al.* 2001; Cao *et al.* 1997b; Sullivan *et al.* 1995

- AG1121: SHIV-HXBc2 is a neutralization sensitive nonpathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. Si *et al.* [2001]
- AG1121: Called 1121 – Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4. Cao *et al.* [1997b]
- AG1121: Recognizes monomeric gp120 from T-cell adapted line HXBc2 and primary isolate 89.6 equally well, but 89.6 was three-fold less sensitive to neutralization by AG1121 than HXBc2. Sullivan *et al.* [1995]

No. 1147
MAb ID Ag1211
HXB2 Location Env
Author Location gp120 (V3) (JRFL)
Epitope

B Cell

Neutralizing
Immunogen
Species (Isotype)
Ab Type V3
References Kwong *et al.* 2002
Keywords antibody binding site definition and exposure

- Ag1211: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)

No. 1148
MAb ID B4a1
HXB2 Location Env
Author Location gp120 (V3)
Epitope
Subtype B
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
Research Contact James Robinson, Tulane University Med School, New Orleans, LA, USA
References Cavacini *et al.* 2003; Cavacini *et al.* 2002
Keywords antibody interactions, co-receptor, variant cross-recognition or cross-neutralization

- B4a1: The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. The anti-V3 MAb B4a1 cross-competes with B4e8. Cavacini *et al.* [2003] (**antibody interactions**)
- B4a1: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-gp41 MAb F240 binding was not affected by the binding of the V3 loop MAb B4a1, but preincubation with F240 could enhance B4a1 binding of the R5 isolate. B4a1 reacts with many B clade isolates, and preincubation with sCD4 enhances binding to both the R5 and R5X4 isolates. B4a1 increased binding of CD4i MAbs 48d, 17b and A1g8, as well as CD4BS MAbs IgG1b12 and F105 to R5X4 virions, but only A1g8 and IgG1b12 binding was increased by B4a1 to the R5 isolate. Additive affects on neutralizaton of the R5X4 isolate with B4a1 and CD4i MAbs was observed, presumably due to increased exposure of the CD4i binding site, but not for the R5 isolate. B4a1 had an additive affect on neutralization with 2G12 with the R5X4 virus but not the R5 virus, and did not impact 2F5 neutralization. Cavacini *et al.* [2002] (**antibody interactions**, **co-receptor**, **variant cross-recognition or cross-neutralization**)

No. 1149
MAb ID B4e8 (F425 B4e8)
HXB2 Location Env
Author Location gp120 (V3)
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG2κ)
Ab Type V3
Research Contact Lisa Cavacini, Beth Isreal Deconess Medical Center, Boston MA, USA
References Zwick *et al.* 2003; Liu *et al.* 2003; Cavacini *et al.* 2003
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, co-receptor, variant cross-recognition or cross-neutralization

- B4e8: This MAb binds to the base of the V3 loop, and binds and neutralizes multiple primary isolates. The anti-V3 MAb B4a1 cross-competes with B4e8. B4e8 and 2G12 enhanced each others binding, and gave synergistic neutralization. B4e8 could neutralize R5X4 virus 92HT593 better than 2G12, while 2G12 was better at neutralizing R5 virus 92US660. B4e8 enhanced binding of CD4i MAbs 4.8d, 1.7b, and A1g8 to 92HT593, but only of 48d to the 92US660, and there was only a modest impact of the combination of B4e8 and CD4i MAbs on neutralization. CD4BS MAb IgG1b12 had no effect on B4e8 binding. Anti-gp41 MAb F240 inhibited B4e8 neutralization. Cavacini *et al.* [2003] (**antibody binding site definition and exposure**, **antibody generation**, **antibody interactions**, **co-receptor**, **variant cross-recognition or cross-neutralization**)
- B4e8: The effect of isotype (IgG1 and IgG3) and subtype (IgA) switching of parental F425B4e8 (IgG2)on HIV-1 binding and neutralization was investigated. IgG1-and IgA-F425B4e8 mutants showed virus-specific binding levels and TCLA SF2 isolate compared to the parental IgG2. Comparable levels of neutralization of primary isolates 92HT593 (R5X4) and 92US660 (R5) was achieved by all isotypes and subtypes of F425B4e8. Liu *et al.* [2003] (**variant cross-recognition or cross-neutralization**, **antibody sequence, variable domain**)
- B4e8: Called F425 B4e8. scFv 4KG5 reacts with a conformational epitope that is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JRFL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS

access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V3 MAbs used. Zwick *et al.* [2003] (**antibody interactions**)

No. 1150
MAb ID D27
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type V3
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Otteken *et al.* 1996; Earl *et al.* 1994

- D27: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D27 is one of two MAbs labeled group Ca, that was type-specific for BH8 – D27 fully blocked CD4 binding, and the deletion of the V3 loop abrogated binding. Sugiura *et al.* [1999]
- D27: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp160 revealed that these anti-CD4 MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes. Otteken *et al.* [1996]
- D27: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1151
MAb ID D47
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: Env
Species (Isotype) mouse
Ab Type V3
Research Contact Patricia Earl, NIAID, NIH
References Salzwedel *et al.* 2000; Earl *et al.* 1997; Wyatt *et al.* 1997; Otteken *et al.* 1996; Richardson *et al.* 1996; Earl *et al.* 1994
Keywords antibody binding site definition and exposure, antibody generation, variant cross-recognition or cross-neutralization

- D47: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – V3 MAb D47 is strain specific and can inhibit sCD4 mediated infection, but only of the closely related LAV Env, while anti-CD4i MAbs were broadly cross-neutralizing. Salzwedel *et al.* [2000] (**variant cross-recognition or cross-neutralization**)
- D47: Used for comparison in a study of gp41 antibodies – D47 binds to a greater extent to cell surface expressed Env than any of 38 conformation dependent anti-gp41 MAbs. Earl *et al.* [1997]
- D47: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. Wyatt *et al.* [1997] (**antibody binding site definition and exposure**)
- D47: Pulse label experiments of MAb binding to noncleavable gp160 revealed that this anti-V3 MAb bound immediately and binding stayed constant through chase period. Otteken *et al.* [1996]
- D47: Used for capture of oligomeric Env for antigen capture ELISA – binding of this antibody to oligomeric Env IIIB was not blocked by human sera from the US, consistent with a low prevalence of IIIB-like V3 strains. Richardson *et al.* [1996] (**antibody binding site definition and exposure**)
- D47: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994] (**antibody generation**)

No. 1152
MAb ID D56
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: vaccinia *Strain:* B clade IIIB
HIV component: oligomeric gp140
Species (Isotype) mouse (IgG)
Ab Type V3
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura *et al.* 1999; Earl *et al.* 1994

- D56: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D56 is one of two MAbs labeled group Ca, that was type-specific for BH8 – D56 fully blocked CD4 binding, and the deletion of the V3 loop abrogated binding – 12.5 ug/ml of D56 was required to achieve 50% neutralization of HIV-1 NL4-3. Sugiura *et al.* [1999]
- D56: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. Earl *et al.* [1994]

No. 1153
MAb ID F5.5
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen
Species (Isotype) mouse
Ab Type V3
Research Contact Hybridolabs, Institute Pasteur
References Altmeyer *et al.* 1999

B Cell

- F5.5: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 Env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies. Altmeyer *et al.* [1999]

No. 1154
MAb ID G3-1472
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
Ab Type V3
Research Contact M. Fung
References Moore & Sodroski 1996

- G3-1472: Binds to carboxy-terminal side of the V3 loop – reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – reciprocal enhanced binding of some anti-V2 MAbs and anti-CD4 binding site MAbs – binding inhibited by anti-C4 MAbs. Moore & Sodroski [1996]

No. 1155
MAb ID K24
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen
Species (Isotype) mouse
Ab Type V3
Research Contact Hybridolabs, Institute Pasteur
References Altmeyer *et al.* 1999

- K24: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies. Altmeyer *et al.* [1999]

No. 1156
MAb ID TH1
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L (MN, J
Immunogen
Species (Isotype) human (IgG1λ)
Ab Type V3
Research Contact Michael Fung, Tanox Biosystem, USA
References Gorny & Zolla-Pazner 2004; Yang *et al.* 1998; D'Souza *et al.* 1995

Keywords assay development, review, variant cross-recognition or cross-neutralization

- TH1: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. TH1 neutralizes some TCLA strains. Gorny & Zolla-Pazner [2004] (**review**)
- TH1: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. Yang *et al.* [1998] (**assay development**)
- TH1: Found to neutralize MN and JRCSF, but not two B subtype primary isolates, nor a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs. D'Souza *et al.* [1995] (**variant cross-recognition or cross-neutralization**)

No. 1157
MAb ID anti-gp120/V3
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *Strain:* A clade 94UG018 *HIV component:* Gag, gp120, Nef, Pol
Species (Isotype) mouse (IgG)
Ab Type V3
Research Contact Intracel Co
References Buonaguro *et al.* 2001

- Anti-V3: HIV-1 pr55 gag-based virus-like particles (VLP) carrying Nef and Pol open reading frames as well as gp120 of the clade A isolate 94UG018 were created using a Baculovirus expression system to package additional ORFS into the VLP – anti-V3 and anti-p24 antibodies were used to assess the expression levels and Gag and gp120-TM were found to be expressed at comparable levels on the VLP. Buonaguro *et al.* [2001]

No. 1158
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* CD4BS, Gag, V3
Species (Isotype) mouse
Ab Type V3
References Truong *et al.* 1996

- Antibodies raised against recombinant anti-p55 virus-like particles with the p24 region 196-226 deleted, bearing inserts of either the V3 or the CD4BS regions of gp120 were studied – no neutralizing responses, weak Env, and strong Gag responses were elicited – the major homology region (MHR) and proximal sequences was found to be required for capsid assembly. Truong *et al.* [1996]

No. 1159
MAb ID polyclonal
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing yes
Immunogen Vaccine
Vector/Type: canarypox prime with recombinant protein boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Pol *Adjuvant:* MF59
Species (Isotype) human
Ab Type V3
References Verrier *et al.* 2000

- Serum Abs elicited by this vaccine reacted with V3 peptides from clades B, C, and F, reacted weakly with V3 peptides from clades A, D, G, and H, and did not react with V3 peptides from clades E and O – neutralizing activity against 5 of 14 primary isolates tested was observed, including one B clade X4 virus, two dualtropic B clade viruses (from clade B) and one clade B and one clade C R5 virus. Verrier *et al.* [2000]

No. 1160
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (303–325)
Epitope
Neutralizing no
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgM)
Ab Type V3
References Sidorova 1999

- Polyspecific anti-MN-24 antibodies were raised through V3 peptide, MN-24 stimulation of human cells, followed by EBV transformation: they react with homologous and heterologous peptides and may be autoantibodies. Sidorova [1999]

No. 1161
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing
Immunogen
Species (Isotype) human
Ab Type V3
References Guevara *et al.* 2002

- Viral RNA in serum and high titers of subtype C consensus V3 peptide binding Abs were the best independent predictors of mother to infant transmission of HIV-1 subtype C – NAb to subtype B HIV-1 (MN) was also correlated. Guevara *et al.* [2002]

No. 1162
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: HIV-1 captured on concavalin A-immobilized polystyrene nanospheres, Con A-NS *Strain:* B clade IIIB *HIV component:* gp120, heat-inactivated virus *Adjuvant:* concavalin A-immobilized polystyrene nanospheres
Species (Isotype) mouse (IgA)
Ab Type V3
References Kawamura *et al.* 2002

- Vaginal fluids were collected after intravaginal immunization of BALB/c mice and analyzed for their anti-HIV-1 antibody levels using a IIIB-V3 ELISA and IIIB neutralization assay – HIV-1 specific IgG was undetectable but anti-HIV IgA antibody response was identified in the vaginal fluids of immunized mice with HIV concavalin A-immobilized polystyrene nanosheres. Kawamura *et al.* [2002]

No. 1163
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype B
Neutralizing L
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade 89.6P, B clade MN *HIV component:* Env *Adjuvant:* aluminum hydroxide, Cholera toxin (CT), GM-CSF, IL-12, IL-18, IL-1α
Species (Isotype) human (IgA, IgG1, IgG2a)
Ab Type V3
References Bradney *et al.* 2002

- The cytokine-adjuvant combination IL-1alpha, IL-12 and IL-18 were found to stimulate potent mucosal antibody responses upon intranasal immunization of mice – cholera toxin is the most widely used adjuvant, but is not safe for use in humans. Bradney *et al.* [2002]

No. 1164
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Subtype C
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* multiple epitope immunogen *HIV component:* V3 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse
Ab Type V3
References Hewer & Meyer 2002

- A synthetic peptide immunogen designated a multiple epitope immunogen (MEI) was generated by synthesizing peptides with mixtures of frequently found amino acids (>10%) from the C subtypes allowed in the synthetic peptide – when injected into mice, the C subtype MEI induced antibodies that recognized the immunogen and whole virus as an antigen in ELIZAs – sera

from eight HIV positive South Africans recognized the MEI peptide in ELISA tests. Hewer & Meyer [2002]

No. 1165
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (V3)
Epitope
Subtype B, C, F
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
Ab Type V3
References Bongertz *et al.* 2003
Country Brazil
Keywords inter-clade comparisons, rate of progression

- Ab responses at diluations above 1:1000 against the consensus V3 loops of subtypes A, B, C, D, F, and Brazilian B and F, were detected in only 6/60 individuals infected with HIV by sexual exposure, while a significantly higher (38/46) reactivity and frequency of peptide recognition was observed in the plasma of IDUs. High Ab titers (> 1:10,000) were directed against V3B, V3Bbr and V3F peptides. The IDU group also displayed broader NAb responses, in comparison to the sexually transmitted group. This may contribute to a slower disease progression in IDUs. Bongertz *et al.* [2003] (**inter-clade comparisons**, **rate of progression**)

No. 1166
MAb ID polyclonal
HXB2 Location Env
Author Location Env
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: adenovirus *Strain:* B clade HXB2/Bal *HIV component:* gp140ΔCFI, gp140ΔV1V2ΔCFImodifiedV3
Species (Isotype) guinea pig (IgG)
Ab Type V3
References Yang *et al.* 2004
Keywords co-receptor

- Neutralizing antibodies against V3 with greater breadth among B clade viruses were created in vaccinated guinea pigs using a combination gp140ΔV1V2 and shortened V3 loop envelope than using intact Envelope. The interior V3 glycosylation site was removed in the modification of V3. This change also caused the virus to become CXCR4 tropic. Yang *et al.* [2004] (**co-receptor**)

No. 1167
MAb ID 11/75a/21/41
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen
Species (Isotype)
Ab Type V3 discontinuous
References Peet *et al.* 1998; McKeating *et al.* 1992a

- 11/75a/21/41: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 11/75a/21/41 binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]

No. 1168
MAb ID 41.1 (ICR41.1i, ICR41)
HXB2 Location Env
Author Location gp120 (HXB10)
Epitope
Neutralizing L (HXB2)
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: gp120
Species (Isotype) rat (IgG2a)
Ab Type V3 discontinuous
Research Contact J. Cordell, Institute for Cancer Research, Sutton, Surrey, UK
References Ugolini *et al.* 1997; Jeffs *et al.* 1996; Armstrong *et al.* 1996; Armstrong & Dimmock 1996; McLain & Dimmock 1994; Klasse *et al.* 1993a; McKeating *et al.* 1993b; McKeating *et al.* 1992a; Reitz *et al.* 1988

- 41.1: Viral binding inhibition by 41.1 was weakly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997]
- 41.1: Called ICR41.1i – IgG2c? – Neutralization was affected if the Ab was added after the virus bound to the host cells at 24 degrees C or below. Armstrong & Dimmock [1996]
- 41.1: Called ICR41.1i – Neutralization occurs by blocking a post-fusion internalization event, in contrast to MAb F58. Armstrong *et al.* [1996]
- 41.1: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120. Jeffs *et al.* [1996]
- 41.1: Called ICR41.1i – Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively – neutralization mediated by 3 molecules of IgG per virion – most efficient at neutralization of the three MAbs studied – acts with multi-hit kinetics. McLain & Dimmock [1994]
- 41.1: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 41.1 is not affected. Klasse *et al.* [1993a]; Reitz *et al.* [1988]

No. 1169
MAb ID 55/45a/1l
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen

Species (Isotype)
Ab Type V3 discontinuous
References Peet *et al.* 1998

- 55/45a/11: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/45a/11 binding was only marginally diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. Peet *et al.* [1998]

No. 1170
MAb ID 1108
HXB2 Location Env
Author Location Env (987)
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type V3 mimotope
References Gorny *et al.* 2004; Gorny & Zolla-Pazner 2004; Zolla-Pazner *et al.* 1999b; Zolla-Pazner *et al.* 1999a
Keywords antibody binding site definition and exposure, antibody generation, mimotopes, review

- 1108: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. Gorny & Zolla-Pazner [2004] (**review**)
- 1108: V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting antigenic conformation is important. This MAb was selected using V3 peptides. Gorny *et al.* [2004] (**antibody binding site definition and exposure**)
- 1108: Selected with peptide 987, a mimotope of anti-V3 MAb 447-D – MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. Zolla-Pazner *et al.* [1999b] (**antibody binding site definition and exposure**, **antibody generation**, **mimotopes**)
- 1108: The sequence of peptide 987, used to select MAb 1108, is ADGAWRSVHLGPGRGSGSGMGK. Zolla-Pazner *et al.* [1999a] (**antibody binding site definition and exposure**, **antibody generation**)

No. 1171
MAb ID polyclonal
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Cholera toxin (CT)
Species (Isotype) rabbit
Ab Type V3-C4
References Zinckgraf *et al.* 1999

- Nasal mucosal immunization and boosting of HIV peptide and was superior for inducing serum IgG and vaginal secretory IgA compared to nasal immunization and vaginal boosting – vaginal immunization and boosting resulted low serum IgG and vaginal IgA and a high vaginal IgG response. Zinckgraf *et al.* [1999]

No. 1172
MAb ID polyclonal
HXB2 Location Env
Author Location
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgA, IgG)
Ab Type V3, V4
References Skott *et al.* 1999

- IgA and IgG from 45 HIV+ individuals was studied – people with low CD4+ cell counts had decreased levels IgA in saliva – sera and saliva IgA was primarily directed toward Env – peptide ELISA studies indicated that teh dominant IgA epitopes were the V4 region (aa 385-409) and the C-term part of the V3 loop (aa 325-344), while the IgG response was directed towards the tip of the loop (aa 308-325) Skott *et al.* [1999]

No. 1173
MAb ID polyclonal
HXB2 Location Env
Author Location gp41
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* gp41
Species (Isotype) rabbit (IgG)
Ab Type alpha-helical hairpin intermediate
References Louis *et al.* 2003
Keywords vaccine antigen design

- Polyclonal Abs raised against soluble trivalently linked N35CCG-N13 and N34CCG, the internal trimeric core of the coiled-coil ectodomain, inhibit HIV-1 Env-mediated cell fusion at levels comparable to 2G12. Louis *et al.* [2003] (**vaccine antigen design**)

No. 1174
MAb ID 2G12 (c2G12)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L P
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type carbohydrates at glycosylation residues in C2, C3, C4, and V4

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References Wang *et al.* 2004; Safrit *et al.* 2004; Pugach *et al.* 2004; Pinter *et al.* 2004; Opalka *et al.* 2004; Nabatov *et al.* 2004; Lorin *et al.* 2004; Liao *et al.* 2004; Jeffs *et al.* 2004; Biorn *et al.* 2004; Gorny & Zolla-Pazner 2004; Pantophlet *et al.* 2003b; Zwick *et al.* 2003; Wolbank *et al.* 2003; Ohagen *et al.* 2003; Montefiori *et al.* 2003; Louis *et al.* 2003; Kitabwalla *et al.* 2003; Raja *et al.* 2003; Singh *et al.* 2003; Wang 2003; Richman *et al.* 2003; Mascola 2003; Hart *et al.* 2003; Ferrantelli *et al.* 2003; Dey *et al.* 2003; Cavacini *et al.* 2003; Binley *et al.* 2003; Abrahamyan *et al.* 2003; Albu *et al.* 2003; Herrera *et al.* 2003; Pantophlet *et al.* 2003a; Stiegler *et al.* 2002; Kwong *et al.* 2002; Gorry *et al.* 2002; Cavacini *et al.* 2002; Bures *et al.* 2002; Liu *et al.* 2002; Ferrantelli & Ruprecht 2002; Zhang *et al.* 2002; Mascola 2002; Grundner *et al.* 2002; Edwards *et al.* 2002; Armbruster *et al.* 2002; Chakrabarti *et al.* 2002; Xu *et al.* 2002; Yang *et al.* 2002; Schulke *et al.* 2002; Scanlan *et al.* 2002; Sanders *et al.* 2002; Golding *et al.* 2002b; Savarino *et al.* 2001; Xu *et al.* 2001; Hofmann-Lehmann *et al.* 2001; Spenlehauer *et al.* 2001; Stiegler *et al.* 2001; Verrier *et al.* 2001; Zeder-Lutz *et al.* 2001; Poignard *et al.* 2001; Moore *et al.* 2001; Barnett *et al.* 2001; Zwick *et al.* 2001c; Mascola & Nabel 2001; Si *et al.* 2001; Park *et al.* 2000; Grovit-Ferbas *et al.* 2000; Baba *et al.* 2000; Robert-Guroff 2000; Binley *et al.* 1999; Mascola *et al.* 2000; Mascola *et al.* 1999; Parren *et al.* 1999; Poignard *et al.* 1999; Crawford *et al.* 1999; Altmeyer *et al.* 1999; Beddows *et al.* 1999; Montefiori & Evans 1999; Schonning *et al.* 1998; Kunert *et al.* 1998; Frankel *et al.* 1998; Wyatt & Sodroski 1998; Li *et al.* 1998; Parren *et al.* 1998b; Takefman *et al.* 1998; Fouts *et al.* 1998; Trkola *et al.* 1998; Binley *et al.* 1998; Connor *et al.* 1998; Sullivan *et al.* 1998b; Parren *et al.* 1998a; Mondor *et al.* 1998; Wyatt *et al.* 1998; Andrus *et al.* 1998; Parren *et al.* 1997b; Burton & Montefiori 1997; Ugolini *et al.* 1997; Mascola *et al.* 1997; Moore & Trkola 1997; Li *et al.* 1997; Fouts *et al.* 1997; Binley *et al.* 1997a; Mo *et al.* 1997; D'Souza *et al.* 1997; Sattentau 1996; Trkola *et al.* 1996a; Poignard *et al.* 1996b; Moore & Sodroski 1996; Trkola *et al.* 1996b; McKeating 1996; McKeating *et al.* 1996; Moore & Ho 1995; Trkola *et al.* 1995; Buchacher *et al.* 1994

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- 2G12: UK Medical Research council AIDS reagent: ARP3030.
- 2G12: NIH AIDS Research and Reference Reagent Program: 1476.
- 2G12: The peptide 12p1 (RINNIPWSEAMM) inhibits direct binding of YU2 gp120 or Env trimer to CD4, CCR5 and MAb 17b in a concentration-dependent allosteric manner. 12p1 is thought to bind to unbound gp120 near the CD4 binding site, with a 1:1 stoichiometry. 12p1 also inhibited MAb F105 binding. presumably because F105 favors an unactivated conformation, but not MAbs 2G12 or b12. The 1:1 stoichiomtry, the fact that the peptide binding site is accessible on the trimer, the non-CD4 like aspect of the binding, and an ability to inhibit viral infection in cell cultures make it a promising lead for therapeutic design. Biorn *et al.* [2004]
- 2G12: This paper is a reviw of anti-HIV-1 Envelope antibodies. This unique epitope is formed from carbohydrates. The mechanism of MAb neutralization is thought to be steric inhibition of CCR5 binding. 2G12 neutralizes many TCLA strains and about 40% of primary isolates tested. Gorny & Zolla-Pazner [2004] (**review**)
- 2G12: A set of oligomeric envelope proteins were made from six primary isolates for potenial use as vaccine antigens: 92/UG/037 (clade A), HAN2/2 (clade B), 92/BR25/025 (clade C), 92/UG/021 (clade D), 93/BR/029 (clade F) and MVP5180 (clade O). This was one of a panel of MAbs used to explore folding and exposure of well characterized epitopes. The clade C isolate BR25 is apparently misfolded, as conformation-dependent antibodies did not bind to it. 2G12 bound to clade A, B, D and F HIV-1 primary isolates. Polyclonal sera raised in rabbits against these antigens cross-bound the other antigens, but none of the sera had neutralizing activity. Jeffs *et al.* [2004] (**vaccine antigen design**, **inter-clade comparisons**)
- 2G12: 2G12 was used as a positive control in a study that showed that A32-rgp120 complexes open up the CCR5 co-receptor binding site, but did not induce neutralizing antibodies with greater breadth among B subtype isolates than did uncomplexed rgp120 in vaccinated guinea pigs. Liao *et al.* [2004] (**vaccine antigen design**)
- 2G12: Mice susceptible to MV infection were intraperitoneally immunized with native HIV-1 89.6 env gp160 and gp140 and δV3 HIV-1 89.6 mutants expressed in live attenuated Schwarz measles vector (MV). The gp160ΔV3 construct raised more cross-reactive NAbs to primary isolates. A HIVIG/2F5/2G12 combination was used as a positive control and could neutralize all isolates. Lorin *et al.* [2004] (**vaccine antigen design**)
- 2G12: A set of HIV-1 chimeras that altered V3 net charge and glycosylation patterns in V1V2 and V3, involving inserting V1V2 loops from a late stage primary isolate taken after the R5 to X4 switch, were studied with regard to phenotype, co-receptor usage, and MAb neutralization. The loops were cloned into a HXB2 envelope with a LAI viral backbone. It was

observed that the addition of the late-stage isolate V1V2 region and the loss of V3-linked glycosylation site in the context of high positive charge gave an X4 phenotype. R5X4 viruses were more sCD4 and 2G12 neutralization resistant than either R5 or X4, but the opposite pattern was observed for b12. Addition of the late stage V1V2 altered neutralization for both MAbs, but this alteration was reversed with the loss of the V3 glycan. Nabatov *et al.* [2004] (**antibody binding site definition and exposure**, **co-receptor**)

- 2G12: An antigen panel representing different regions of gp41 was generated, and sera from 23 individuals were screened. 2G12 was a control, binding to gp120 but to none of the gp41 peptides in the experiment. Opalka *et al.* [2004] (**assay development**, **assay standardization/improvement**)
- 2G12: V1V2 was determined to be the region that conferred the neutralization phenotype differences between two R5-tropic primary HIV-1 isolates, JRFL and SF162. JRFL is resistant to neturalization by many sera and MAbs, while SF162 is sensitive. All MAbs tested, anti-V3, -V2, -CD4BS, and -CD4i, (except the broadly neutralizing MAbs IgG1b12, 2F5, and 2G12, which neutralized both strains), neutralized the SF162 pseudotype but not JRFL, and chimeras that exchanged the V1V2 loops transferred the neutralization phenotype. 2G12 was the only MAb that neutralized JRFL more efficiently than SF162, with a 6-fold lower ND50 for JRFL. 2G12 also had ahigher affinity for JRFL. Pinter *et al.* [2004] (**variant cross-recognition or cross-neutralization**)
- 2G12: A primary isolate, CC1/85, was passaged 19 times in PBMC and gradually acquired increased sensitivity to FAb b12 and sCD4 that was attributed to changes in the V1V2 loop region, in particular the loss of a potential glycosylation site. The affinity for sCD4 was unchanged in the monomer, suggesting that the structural impact of the change was manifested at the level of the trimer. The passaged virus, CCcon19, retained an R5 phenotype and its neutralization susceptibility to other Abs was essentially the same as CC1/85. The IC50 for 2G12 was 1.8 for CC1/85, and was 4.2 for CCcon19, so both the primary and passaged viruses were neutralized. Pugach *et al.* [2004] (**reversion, viral fitness**, **variant cross-recognition or cross-neutralization**)
- 2G12: This review discusses research presented at the Ghent Workshop of prevention of breast milk transmission and immunoprophylaxis for HIV-1 in pediatrics (Seattle, Oct. 2002), and makes the case for developing passive or active immunoprophylaxis in neonates to prevent mother-to-infant transmission. Macaque studies have shown that passive transfer of NAb combinations (for example, IgG1b12, 2G12, 2F5, and 4E10; or 2G12 and 2F5) can confer partial or complete protection to infant macaques from subsequent oral SHIV challenge. Safrit *et al.* [2004] (**immunoprophylaxis**, **mother-to-infant transmission**)
- 2G12: Synthetic mannose Man9 clusters arranged on a scaffold were used to mimic the epitope of 2G12. Bi-, tri, and tetra-valent clusters had a 7-, 22-, and 73-fold higher affinities for 2G12 than the monomers, suggesting that 2G12 binds best to multiple carbohydrate moieties. 2G12 bound larger mannose oligosaccharides with higher affinity: Ma9GlcNAc bound 210- and 74-fold more effectively that Man6GlcNac and Man5GlcNAc, respectively. Wang *et al.* [2004] (**antibody binding site definition and exposure**)
- 2G12: SOS-Env is a mutant protein engineered to have a disulfid bond between gp120 and gp41. Cells expressing SOS-Env due not fuse with target cells expressing CD4 and CCR5, although the fusion process proceeds to an intermediate state associated with CD4 and co-receptors, prior to the formation of the six helix bundle that allows fusion.2G12 was used to monitor surface expression of SOS-Env compared to wildtype. Abrahamyan *et al.* [2003] (**co-receptor**, **vaccine antigen design**)
- 2G12: 2G12 was used as a positive control to test for a NAb activity in mice intranasally immunized with gp120 or gp140 with IL-12 and Cholera Toxin B. Albu *et al.* [2003]
- 2G12: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. 2G12 is able to neutralize both the wildtype and SOS protein comparably, but 2G12 could not neutralize SOS when added post-attachment. Binley *et al.* [2003] (**vaccine antigen design**)
- 2G12:The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. B4e8 and 2G12 enhanced each others binding, and gave synergistic neutralization. B4e8 could neutralize R5X4 virus 92HT593 better than 2G12, while 2G12 was better at neutralizing R5 virus 92US660. Cavacini *et al.* [2003] (**antibody interactions**)
- 2G12: A sCD4-17b single chain chimera was made that can bind to the CD4 binding site, then bind and block co-receptor interaction. This chimeric protein is a very potent neutralizing agent, more potent than IgG1b12, 2G12 or 2F5 against Ba-L infection of CCR5-MAGI cells. It has potential for prophylaxis or therapy. Dey *et al.* [2003] (**co-receptor**)
- 2G12: Four newborn macaques were challenged with pathogenic SHIV 89.6 and given post exposure prophylaxis using a combination of NAbs 2F5, 2G12, 4E10 and IgG1b12. 2/4 treated animals did not show signs of infection, and 2/4 macaques maintained normal CD4+ T cell counts and had a lower delayed peak viremia compared to the controls. Ferrantelli *et al.* [2003] (**immunoprophylaxis**, **mother-to-infant transmission**)
- 2G12: This study investigates the effects of glycosylation inhibitors on the binding between HIV-1 gp120 and mannose-binding lectin (MBL). Mannosidase I inhibitor deoxymannojirimycin (dMM) inhibits formation of complex and hybrid N-linked saccharides and yields virus with more mannose residues. dMM added during viral production significantly enhanced the binding 2F5 and 2G12, but not IgG1b12 in a viral capture assay. Hart *et al.* [2003] (**antibody binding site definition and exposure**)
- 2G12: CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (non-neutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the non-neutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 –

2G12 was used to normalize and as a control in these experiments. Herrera *et al.* [2003] (**antibody interactions**)

- 2G12: MAbs IgG1b12, 2G12, 2F5 and 4E10 were tested for their ability to neutralize two primary HIV-1 clade A isolates (UG/92/031 and UG/92/037) and two primary HIV-1 clade D isolates (UG/92/001 and UG/92/005). 4E10 demonstrated the most potent cross-neutralization activity. Quadruple administration of MAbs IgG1b12, 2G12, 2F5, and 4E10 induced strong synergistic neutralization of 4 clade A isolates (UG/92/031, UG/92/037, RW/92/020 and RW/92/025) as well as 5 clade D isolates (UG/92/001,UG/9/005, /93/086/RUG/94/108, UG/94/114). The authors note this combination of 4 MAbs neutralizes primary HIV A, B, C, and D isolates. Kitabwalla *et al.* [2003] (**antibody interactions**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **mother-to-infant transmission**, **inter-clade comparisons**)
- 2G12: Polyclonal Abs raised against soluble trivalently linked N35CCG-N13 and N34CCG, the internal trimeric core of the coiled-coil ectodomain, inhibit HIV-1 Env-mediated cell fusion at levels comparable to 2G12. Louis *et al.* [2003] (**vaccine antigen design**)
- 2G12: This review dicusses the importance and function of protective antibody responses in animal model studies in the context of effective vaccine development. SHIV models have shown protection using high levels of MAbs can prevent infection, and partial protection that can influence disease course can be obtained from modest levels of NAbs. SHIV challenges studies conducted with infusions of combinations of MAbs b12, 2G12, and 2F5 are reviewed. Mascola [2003] (**immunoprophylaxis**, **review**)
- 2G12: AC10 is a subject who was given treatment early after infection, and had a viral rebound after cessation of therapy, which then declined to a low level. The polyclonal sera from AC10 could potently neutralize the rebound virus, and NAb escape followed with a neutralizing response against the escape variant and subsequent escape from that response. Viral loads remained low in this subject despite escape. The rebound isolate that was potently neutralized by autologous sera was not particularly neutralization sensitive, as it resisted neutralization by sCD4 and MAbs IgG1b12, 2G12 and 2F5, and was only moderately sensitive to sera from other HIV+ individuals that had high titers of NAbs to TCLA strains. Montefiori *et al.* [2003] (**acute infection**, **escape**)
- 2G12: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. 2G12 was the only MAb tested to recognize all blood and brain isolates from all four patients by gp120 immunoprecipitation. Ohagen *et al.* [2003] (**variant cross-recognition or cross-neutralization**)
- 2G12: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded. Pantophlet *et al.* [2003a] (**antibody binding site definition and exposure**)
- 2G12: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. Pantophlet *et al.* [2003b] (**vaccine antigen design**)
- 2G12: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs IgG1b12, F91 and F105 and their Fab counterparts (except for C11, used as a negative control) inhibited CD4-independent JR-FL and YU-2 gp120-CCR5 binding to CCR5-expressing Cf2Th cells and syncytium formation. The carbohydrated binding MAb 2G12 also inhibited CD4-independent syncytium formation. Raja *et al.* [2003] (**co-receptor**)
- 2G12: Most plasma samples of patients from early infection had NAb responses to early autologous viruses, and NAbs against heterologous strains tended to be delayed. Serial plasma samples were tested against serial isolates, and neutralization escape was shown to be rapid and continuous throughout infection. Autologous neutralization-susceptible and resistant viruses from four patients were tested for susceptability to neutralizing Ab responses using MAbs 2G12, IgG1b12 and 2F5. No correlation was established, all viruses tested were susceptible to at least one of the neutralizing MAbs. Two patients that did not have an autologous NAb response also did not evolve changes in susceptibility to these MAbs, while one patient with a pattern of autologous neutralization and escape acquired a 2G12 sensitive virus at month 6, and lost IgG1b12 sensitivity at month 21. Richman *et al.* [2003] (**autologous responses**, **acute infection**, **escape**)
- 2G12: To begin to design vaccine antigens that can mimic the carbohydrate structure, the gp120 peptide 336-342 was synthesized with Man(9), Man(6), and Man(5) moieties attached. Singh *et al.* [2003] (**vaccine antigen design**)
- 2G12: Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. They have shown that both N-glycans, at 295N and 332N are required for 2G12 binding, emphasizing the oligosaccharide cluster nature of the epitope, and suggest the uniqueness of the target structure may not result in autoimmune reactions. Wang [2003] (**vaccine antigen design**, **review**)
- 2G12: The broadly neutralizing antibodies 2F5 and 2G12 were class-switched from IgG to IgA and IgM isotypes. Neutralizing potency was increased with valence for 2G12 so the IgM form was most potent, but for 2F5 the IgG form was most potent. Eight primary isolates were tested including two subtype A isolates. The polymeric IgM and IgA Abs, but not the corresponding IgGs, could interfere with HIV-1 entry across a mucosal epithelial layer, although they were limited in a standard neutralization assay. All isotypes could interact with activated human sera, presumably through complement, to inhibit HIV repli-

cation. Wolbank *et al.* [2003] (**complement**, **isotype switch**, **variant cross-recognition or cross-neutralization**, **mucosal immunity**, **inter-clade comparisons**)

- 2G12: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. 2G12 had no impact on 4KG5 binding. Zwick *et al.* [2003] (**antibody interactions**)
- 2G12: A phase I trial in seven HIV+ individuals was conducted with MAbs 2F5 and 2G12 – no clinical or laboratory abnormalities were observed throughout the study – eight infusions were administered over a 4-week period (total dose 14 g) – the elimination half-life ($t\_1/2$) was calculated to be 7.94 (range, 3.46–8.31) days for 2F5 and 16.48 (range, 12.84–24.85) days for 2G12. Armbruster *et al.* [2002] (**kinetics**, **immunotherapy**)
- 2G12: IgG1b12 neutralized many South African (5/8) and Malawian (4/8) clade C primary HIV-1 isolates, being more effective than 2F5 which neutralized only two Malawian and no South African isolates. 2G12 did not neutralize any of the 16 isolates. Bures *et al.* [2002] (**inter-clade comparisons**)
- 2G12: This study examined Ab interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-gp41 MAb F240 did not affect binding of 2G12 to either R5X4 and R5 isolates, and anti-V3 MAb B4a1 increased 2G12 binding to R5X4 virions but not R5. Neutralization with B4al and 2G12 was additive for the R5X4 virus, and was enhanced for the R5 virus. Cavacini *et al.* [2002] (**antibody interactions**, **co-receptor**, **variant cross-recognition or cross-neutralization**)
- 2G12: A modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. Chakrabarti *et al.* [2002] (**vaccine antigen design**)
- 2G12: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. Edwards *et al.* [2002] (**antibody binding site definition and exposure**)
- 2G12: Review of NAbs that notes 2G12 alone or in combination with other MAbs can protect some macaques against SHIV infection, that it has strong ADCC activity, and that it is safe and well tolerated in humans. Ferrantelli & Ruprecht [2002] (**immunoprophylaxis**)
- 2G12: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. Golding *et al.* [2002b] (**antibody binding site definition and exposure**)
- 2G12: UK1-br and MACS2-br are R5 isolates derived from brain tissue samples from AIDS patients with dementia and HIV-1 encephalitis; both are neurotropic, but only UK1-br induced neuronal apoptosis and high levels of syncytium formation in macrophages. UK1-br Env had a greater affinity for CCR5 than MACS-br, and required low levels of CCR5 and CD4 for cell-to-cell fusion and single round infection. PBMC infected with UK1-br and MACS2-br virus isolates were resistant to neutralization by MAb 2G12. UK1-br was more sensitive than MACS2-br to IgG1b12, 2F5 and CD4-IgG2 neutralization. Gorry *et al.* [2002] (**brain/CSF**, **co-receptor**)
- 2G12: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads, while such an affinity difference was not seen with F105 and 2G12 – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface. Grundner *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 2G12: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, except for 2G12, which might not have bound well to the carbohydrate additions on the Drosophila expressed core. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. The high values suggest surface burial or protein folding an ordering of amino acids. 2G12 had an entropy value of -1.6. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Kwong *et al.* [2002] (**antibody binding site definition and exposure**)
- 2G12: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal

studies, and vaccine strategies. Liu *et al.* [2002] (**review**)

- 2G12: Rhesus macaques were better protected from vaginal challenge with SHIV89.6D (MAb 2G12, 2/4; MAbs 2F5/2G12, 2/5; and HIVIG/2F5/2G12, 4/5 infected) than from intravenous challenge (MAb 2G12, 0/3; MAbs 2F5/2G12, 1/3; and HIVIG/2F5/2G12, 3/6 infected)– the animals that were infected by vaginal challenge after Ab infusion had low or undetectable viral RNA levels and modest CD4 T-cell decline. Mascola [2002] (**immunoprophylaxis**, **mucosal immunity**)
- 2G12: The 2G12 epitope is composed of carbohydrates involving high-mannose and hybrid glycans of residues 295, 332, and 392, with peripheral glycans from 386 and 448 contributing on either flank, and with little direct gp120 protein surface involvement – these mannose residues are proximal to each other near the chemokine receptor binding surface. Sanders *et al.* [2002] (**antibody binding site definition and exposure**)
- 2G12: Alanine scanning mutagenesis used in conjunction with competition and replacement studies of N-linked carbohydrates and sugars suggest that the 2G12 epitope is formed from mannose residues contributed by the glycans attached to N295 and N332, with the other N-linked carbohydrates in positions N339, N386, and N392 playing a role in maintaining conformation relevant to 2G12 binding – N295A and N332A mutants showed essentially unchanged anti-CD4BS NAb b12 binding affinities, while N339A, N386A and N392A mutants displayed significantly lowered b12 affinity, presumably due to conformational changes. Scanlan *et al.* [2002] (**antibody binding site definition and exposure**)
- 2G12: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 – 2G12 complexes with SOS gp140 or with gp120 had a very unusual linear structure. Schulke *et al.* [2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 2G12: The antiviral response to intravenously administered MAbs 2F5 and 2G12 was evaluated in 7 HAART-naïve asymptomatic HIV-1 infected patients during a treatment period of 28 days. MAb therapy reduced plasma HIV RNA in 3/7 patients during the treatment period, and transiently reduced viral load in two more. CD4 counts were up in 3/7 through day 28, and transiently increased in three more. Vigorous complement activation was observed after 48/56 Ab infusions. Virus derived from 2/7 patients could be neutralized by 2G12, and escape from 2G12 was observed in both cases after infusion; one year after the infusion, isolates were again sensitive to 2G12. Stiegler *et al.* [2002] (**complement**, **variant cross-recognition or cross-neutralization**, **escape**, **immunotherapy**)
- 2G12: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. Xu *et al.* [2002] (**antibody interactions**, **immunoprophylaxis**, **mother-to-infant transmission**)
- 2G12: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and MAbs C11, A32, and 30D which did not bind the stabilized oligomer. Yang *et al.* [2002] (**antibody binding site definition and exposure**)
- 2G12: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. Zhang *et al.* [2002] (**antibody binding site definition and exposure**)
- 2G12: SF162DeltaV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization – when incorporated into a codon-optimized DNA vaccine with a CMV promoter and delivered by gene gun, SF162DeltaV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162DeltaV2, but not intact SF162, was used as the immunogen – Control MAbs 2F5 and 2G12 could neutralize all of the following primary isolates: 91US056(R5), 92US714(R5), 92US660(R5), 92HT593(R5X4), and BZ167(R5X4), while after the first protein boost, the sera from two SF162DeltaV2 immunized macaques could neutralize 91US056(R5), 92US714(R5), 92US660(R5) and ADA(R5), but not 92HT593(R5X4) or 92US657(R5) – the pattern of cross-recognition shifted after the second boost. Barnett *et al.* [2001] (**vaccine antigen design**)
- 2G12: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonates macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline. Hofmann-Lehmann *et al.* [2001] (**immunoprophylaxis**, **mother-to-infant transmission**)
- 2G12: Review of studies in macaques that have shown immune control of pathogenic SHIV viremia, improved clinical outcome, and protection, and the implications of the observations for HIV vaccines. Mascola & Nabel [2001] (**review**)
- 2G12: Moore and colleagues review structural aspects of gp120 and how they relate to antigenic domains, and review the data concerning the lack of a clear relationship between genetic subtype and serotype – an exception exists for human MAb 2G12, which does not recognize CRF01 envelopes because of

an unusual additional disulfide bond in the V4 loop region that appears to be unique to the subtype E, CRF01 gp120 protein. Moore *et al.* [2001] (**antibody binding site definition and exposure**, **review**)

- 2G12: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – although it is potently neutralizing, 2G12 does not interfere with CD4 and coreceptor binding, and this Ab specificity is uncommon in sera from HIV-1-infected individuals. Poignard *et al.* [2001] (**antibody binding site definition and exposure**, **review**)
- 2G12: Chloroquine reduces the HIV-1-infectivity of H9 IIIB cells, apparently through altering the conformation of envelope – there is a reduction of reactivity of 2G12 to its epitope in chloroquine treated cultures. Savarino *et al.* [2001] (**antibody binding site definition and exposure**)
- 2G12: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. Si *et al.* [2001]
- 2G12: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12. Spenlehauer *et al.* [2001] (**assay development**)
- 2G12: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001] (**antibody interactions**)
- 2G12: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10. Xu *et al.* [2001] (**antibody interactions**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 2G12: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three MAbs with respect to monomeric and oligomeric Env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers – 2G12-gp160 oligomer interactions were best fitted to a two state model, with the first complex having a high association constant and fast dissociation, stabilized by conformational changes induced by the binding of a second MAb. Zeder-Lutz *et al.* [2001] (**antibody binding site definition and exposure**, **antibody interactions**, **kinetics**)
- 2G12: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 – there was no evidence for cooperativity of binding between b12 and 2G12 to envelope spikes expressed on the cell surface of TCLA or primary isolates. Zwick *et al.* [2001c] (**antibody interactions**)
- 2G12: A triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the mean plasma half-life was 14.0 +/- 7.9 days, the longest of the three Abs. Baba *et al.* [2000] (**immunoprophylaxis**, **mother-to-infant transmission**)
- 2G12: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. Grovit-Ferbas *et al.* [2000] (**vaccine antigen design**)
- 2G12: Because HIV-1 is most often transmitted across mucosal surfaces, the ability of passive transfer of infused HIVIG/2F5/2G12 to protect against mucosal exposure of macaques to pathogenic SHIV 89.6PD was studied – HIVIG/2F5/2G12 protected 4/5 animals against vaginal challenge, 2F5/2G12 combined protected 2/5 animals, and 2G12 alone protected 2/4 animals – in contrast, Mascola and coworkers had previously shown single MAbs could not protect against intervenous challenge – Ab treated animals that got infected through vaginal innoculation had low viral loads and only modest declines in CD4 counts – the infused Abs were detected in the nasal, vaginal, and oral mucosa. Mascola *et al.* [2000] (**immunoprophylaxis**, **mucosal immunity**)
- 2G12: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – 2G12 was an exception and could not neutralize MN in either form. Park *et al.* [2000]
- 2G12: A mini-review of observations of passive administration of IgG NAbs conferring protection against intervenous or vaginal SHIV challenge, that considers why IgG MAbs might protect against mucosal challenge. Robert-Guroff [2000] (**immunoprophylaxis**, **mucosal immunity**, **review**)
- 2G12: A Semliki Forest virus (SFV) expression system carrying BX08 Env was used to study the conformation of gp120

Env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface expressed Env was recognized only by the conformation-dependent Abs and not by anti-V3 Abs. Altmeyer *et al.* [1999]

- 2G12: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 2G12 was able to bind with low affinity to the rgp120 monomer HIV-1 W61D. Beddows *et al.* [1999]
- 2G12: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 2G12: Neutralization assays with rsCD4, MAbs, and serum samples from SHIV-infected macaques and HIV-1 infected individuals were used to characterize the antigenic properties of the env glycoprotein of six primary isolate-like or TCLA SHIV variants. 2G12 neutralized the five SHIV strains tested, HXBc2, KU2, 89.6, 89.6P and KB9, in MT-2 cells. Crawford *et al.* [1999] (**variant cross-recognition or cross-neutralization**)
- 2G12: Combinations of HIVIG, 2F5, 2G12 were administered in passive-transfer experiments 24 hours prior to challenge with pathogenic SHIV 89.6PD – 3/6 animals given HIVIG/2F5/2G12 were completely protected, the others had reduced viremia and normal CD4 counts – 1/3 monkeys given 2F5/2G12 showed transient infection, the other two had reduced viral load – all monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia, although animals that got HIVIG or 2G12 had a less profound CD4 T cell decline. Mascola *et al.* [1999] (**antibody interactions**)
- 2G12: A meeting summary presented results regarding neutralization –MAbs 2G12 and 2F5 tested for their ability to neutralize primary isolate infection of genetically engineered cell lines (cMAGI and others, presented by T. Matthews, A. Trkola, J. Bradac) – an advantage of such cells lines over PBMCs is that markers (X-Gal) can be added for staining to simplify the assay – the consensus of the meeting was that these engineered cell lines did not improve the sensitivity of detection of primary isolate neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization *in vitro* corresponded to efficacy *in vivo*. Montefiori & Evans [1999] (**review**)
- 2G12: Review of the neutralizing Ab response to HIV-1. Parren *et al.* [1999] (**review**)
- 2G12: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice b12 escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs. Poignard *et al.* [1999] (**antibody interactions**, **escape**)
- 2G12: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect when delivered 4 hours post infection. Andrus *et al.* [1998] (**immunoprophylaxis**)
- 2G12: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – MAb 2G12 was the only exception to this, showing reduced binding efficiency. Binley *et al.* [1998] (**antibody binding site definition and exposure**)
- 2G12: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D. Connor *et al.* [1998]
- 2G12: Notes that 2G12 and 2F5, potent neutralizing antibodies, were identified by screening for cell surface (oligomeric Envelope) reactivity. Fouts *et al.* [1998] (**antibody binding site definition and exposure**)
- 2G12: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events. Frankel *et al.* [1998] (**mucosal immunity**)
- 2G12: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods – 2G12 D(H) has the best homology to a D(H) segment between D3-22 and D4-23, a region not usually considered for heavy-chain rearrangement because it lacks associated recombination signals in the flanking regions, Kunert *et al.* suggest this may be why Abs that compete with 2G12 are rare. Kunert *et al.* [1998] (**antibody sequence, variable domain**)

- 2G12: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) Li *et al.* [1998] (**antibody interactions**)
- 2G12: Enhances Hx10 binding to CD4 positive or negative HeLa cells, but inhibited binding to CD4+ T-cell line A3.01 – neutralizes Hx10 infection of the HeLa cells. Mondor *et al.* [1998]
- 2G12: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. Parren *et al.* [1998a] (**antibody binding site definition and exposure**)
- 2G12: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope. Parren *et al.* [1998b] (**variant cross-recognition or cross-neutralization**)
- 2G12: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, 2G12 was found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan and has a mutation at the tip of the loop more efficiently than it neutralizes HIV-BRU. Schonning *et al.* [1998] (**antibody binding site definition and exposure**)
- 2G12: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10. Sullivan *et al.* [1998b] (**antibody interactions**)
- 2G12: Induces complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML. Takefman *et al.* [1998] (**complement**, **variant cross-recognition or cross-neutralization**)
- 2G12: A wide range of neutralizing titers was observed that was independent of co-receptor usage. Trkola *et al.* [1998] (**co-receptor**, **variant cross-recognition or cross-neutralization**)
- 2G12: Summary of the implications of the crystal structure of gp120 combined with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by 2G12 is unknown, but dependent on proper glycosylation and 2G12 is predicted to be oriented toward the target cell when bound, so neutralization may be due to steric hindrance – mutations in positions N 295, T 297, S 334, N 386, N 392 and N 397 HXBc2 (IIIB) decrease 2G12 binding, and the binding region is 25 angstroms from the CD4 binding site – probably the Ab binds in part to carbohydrates, which may account for both its broad reactivity and the scarcity of Abs in the same competition group. Wyatt *et al.* [1998] (**antibody binding site definition and exposure**)
- 2G12: Review of the antigenic and receptor binding-domains of gp120 in relation to the structure of the molecule – MAbs are discussed by category (anti-V2, anti-V3, CD4i, CD4BS...), however as 2G12 binds to a rarely immunogenic region, and it is dependent on glycosylation, it was discussed individually. Wyatt & Sodroski [1998] (**review**)
- 2G12: Review that discusses this MAb – reacts with residues at the base of the V3 loop and V4, and most of the changes that reduce binding are glycosylation sites – it is not clear whether the binding site is peptidic or direct carbohydrate. Burton & Montefiori [1997] (**antibody binding site definition and exposure**, **review**)
- 2G12: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 mug per ml for 90% viral inhibition – neutralized 6 of 9 primary isolates. D'Souza *et al.* [1997] (**variant cross-recognition or cross-neutralization**)
- 2G12: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 2G12 bound monomer, and weakly bound oligomer and neutralized JRFL. Fouts *et al.* [1997] (**antibody binding site definition and exposure**)
- 2G12: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB Env – 2G12 was a strong neutralizer of SHIV-vpu+ – all Ab combinations tested showed synergistic neutralization – 2G12 has synergistic response with MAbs 694/98-D (anti-V3), 2F5, F105, and b12. Li *et al.* [1997] (**antibody interactions**)
- 2G12: Using concentrations of Abs achievable *in vivo*, the triple combination of 2F5, 2G12 and HIVIG was found to be synergistic to have the greatest breadth and magnitude of response against 15 clade B primary isolates. Mascola *et al.* [1997] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 2G12: A JRCSF variant that was selected for IgG1b12 resistance remained sensitive to MAbs 2G12 and 2F5, for combination therapy. Mo *et al.* [1997] (**escape**)
- 2G12: Review: MAbs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes. Moore & Trkola [1997] (**immunoprophylaxis**, **immunotherapy**, **review**)
- 2G12: Neutralizes TCLA strains and primary isolates. Parren *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)
- 2G12: Viral binding inhibition by 2G12 was strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) Ugolini *et al.* [1997] (**antibody binding site definition and exposure**)
- 2G12: Neutralizes primary isolates, HXB2, and chimeric virus with gp120 from primary isolates in an HXB2 background. McKeating *et al.* [1996] (**variant cross-recognition or cross-neutralization**)
- 2G12: Binding weakly enhanced by some anti-C1, -C4, -V3, and CD4 binding site MAbs – unusual in that 2G12 binding neither enhanced or inhibited the binding of other MAbs included in the study. Moore & Sodroski [1996] (**antibody interactions**)
- 2G12: Review: exceptional capacity to neutralize primary isolates in terms of both breadth and potency – one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates. Poignard *et al.*

[1996b] (**variant cross-recognition or cross-neutralization**, **review**)
- 2G12: Review: Only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5. Sattentau [1996] (**review**)
- 2G12: Conformationally sensitive epitope destroyed by mutations altering the N-linked glycosylation sites near the base of the V3 loop and the amino-terminal flank of the V4 loop. Trkola *et al.* [1996b] (**antibody binding site definition and exposure**)
- 2G12: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. Trkola *et al.* [1996a] (**co-receptor**)
- 2G12: Review: binding site is distinct from CD4BS MAbs epitope and is unique among known gp120 MAbs, human or rodent. Moore & Ho [1995] (**review**)
- 2G12: Highly potent Cross-clade neutralizing activity. Trkola *et al.* [1995] (**inter-clade comparisons**)
- 2G12: Human MAb generated by electrofusion of PBL from HIV-1 + volunteers with CB-F7 cells. Buchacher *et al.* [1994] (**antibody generation**)

No. 1175
MAb ID 1367
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type cluster I
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Gorny *et al.* 2000; Gorny & Zolla-Pazner 2000; Nyambi *et al.* 1998
Keywords antibody binding site definition and exposure, inter-clade comparisons, review

- 1367: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. Gorny & Zolla-Pazner [2004] (**review**)
- 1367: A cluster I epitope that binds to rgp41 567-647, recognizes a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41 – this MAb doesn't react with either of the peptides N51 or C43 individually – MAbs 50-69 and 1367 had similar properties. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**)
- 1367: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)
- 1367: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 1367 weakly bound to the majority of isolates – no neutralizing activity was observed when tested with 5 isolates, but 1367 did not bind well to these isolates. Nyambi *et al.* [2000] (**inter-clade comparisons**)
- 1367: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98-6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade. Nyambi *et al.* [1998] (**inter-clade comparisons**)

No. 1176
MAb ID 7B2
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen
Species (Isotype)
Ab Type cluster I
References Binley *et al.* 2003; Binley *et al.* 1999
Keywords antibody binding site definition and exposure, vaccine antigen design

- 7B2: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. gp41 Abs 7B2 and 2.2B did not neutralize in any format, WT, SOS, nor when added postbinding. Binley *et al.* [2003] (**vaccine antigen design**)
- 7B2: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999] (**antibody binding site definition and exposure**)

No. 1177
MAb ID 126-6 (SZ-126.6)
HXB2 Location Env
Author Location gp41 (HXB2)

Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG2κ)
Ab Type cluster II
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny & Zolla-Pazner 2004; Finnegan *et al.* 2002; Nyambi *et al.* 2000; Gorny & Zolla-Pazner 2000; Hioe *et al.* 1997b; Earl *et al.* 1997; Binley *et al.* 1996; Chen *et al.* 1995; Eddleston *et al.* 1993; Xu *et al.* 1991; Robinson *et al.* 1991; Robinson *et al.* 1990b
Keywords antibody binding site definition and exposure, enhancing activity, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization

- 126-6: NIH AIDS Research and Reference Reagent Program: 1243.
- 126-6: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- 126-6: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. Finnegan *et al.* [2002] (**antibody binding site definition and exposure**, **kinetics**)
- 126-6: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone – MAb 126-6 was biotinylated and used as a probe to determine that anti-gp41 MAb 50-69 bound the fusogenic form of the protein in liquid phase. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**)
- 126-6: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs. Nyambi *et al.* [2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 126-6: Discontinuous epitope recognizing residues between 649-668 – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding. Binley *et al.* [1996] (**antibody binding site definition and exposure**)
- 126-6: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation. Chen *et al.* [1995] (**antibody binding site definition and exposure**)
- 126-6: Called SZ-126.6. Eddleston *et al.* [1993]
- 126-6: No enhancing or neutralizing activity. Robinson *et al.* [1991] (**enhancing activity**)
- 126-6: Specific for a conformational epitope. Xu *et al.* [1991] (**antibody binding site definition and exposure**)
- 126-6: No enhancing activity for HIV-1 IIIB. Robinson *et al.* [1990b] (**enhancing activity**)

No. 1178
MAb ID 1342
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type cluster II
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny & Zolla-Pazner 2004; Nyambi *et al.* 2000; Gorny *et al.* 2000; Gorny & Zolla-Pazner 2000; Nyambi *et al.* 1998
Keywords antibody binding site definition and exposure, inter-clade comparisons, review

- 1342: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- 1342: This cluster II MAb is a conformational epitope that binds in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**)
- 1342: Binds within the region gp41 647-682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)
- 1342: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity –

Clade D isolates bound most consistently to cluster II MAbs – no neutralizing activity was observed when tested with 5 isolates, but 1342 did not bind to these isolates. Nyambi *et al.* [2000] (**inter-clade comparisons**)

- 1342: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98-6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade. Nyambi *et al.* [1998] (**inter-clade comparisons**)

No. 1179
MAb ID 1379
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type cluster II
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny & Zolla-Pazner 2004; Gorny *et al.* 2000; Gorny & Zolla-Pazner 2000
Keywords antibody binding site definition and exposure, review

- 1379: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- 1379: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**)
- 1379: Binds within the region gp41 647-682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. Gorny *et al.* [2000] (**antibody binding site definition and exposure**)

No. 1180
MAb ID 2.2B
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen
Species (Isotype)
Ab Type cluster II
Research Contact James Robinson, Tulane University, Tulane, LA
References Binley *et al.* 2003; Schulke *et al.* 2002; Binley *et al.* 1999
Keywords vaccine antigen design

- 2.2B: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. gp41 Abs 7B2 and 2.2B did not neutralize in any format, WT, SOS, nor when added postbinding. Binley *et al.* [2003] (**vaccine antigen design**)
- 2.2B: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140. Schulke *et al.* [2002] (**vaccine antigen design**)
- 2.2B: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. Binley *et al.* [1999] (**vaccine antigen design**)

No. 1181
MAb ID Fab D11 (D11)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review

- Fab D11: Called D11. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab D11: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)

No. 1182
MAb ID Fab D5 (D5)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review

- Fab D5: Called D5. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab D5: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)

No. 1183
MAb ID Fab G1
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review

- Fab G1: Called G1. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab G1: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)

No. 1184
MAb ID Fab M10
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Parren *et al.* 1997b; Binley *et al.* 1996

- Fab M10: Does not bind to MN native oligomer, but does bind to both LAI and MN rgp120 and rgp140. Parren *et al.* [1997b]
- Fab M10: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996]

No. 1185
MAb ID Fab M12 (M12)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review

- Fab M12: Called M12. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab M12: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)

No. 1186
MAb ID Fab M15
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords review

- Fab M15: Called M15. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab M15: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996]

No. 1187
MAb ID Fab S10 (S10)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996

Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab S10: Called S10. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab S10: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 1188
MAb ID Fab S6 (S6)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, review

- Fab S6: Called S6. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab S6: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody interactions**, **antibody sequence, variable domain**)

No. 1189
MAb ID Fab S8 (S8)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, review

- Fab S8: Called S8. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab S8: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody interactions**, **antibody sequence, variable domain**)

No. 1190
MAb ID Fab S9 (S9)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, review

- Fab S9: Called S9. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab S9: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody interactions**, **antibody sequence, variable domain**)

No. 1191
MAb ID Fab T3 (T3)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster II
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab T3: Called T3. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab T3: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 1192
MAb ID Md-1 (MD-1)
HXB2 Location Env
Author Location gp41

Epitope
Neutralizing no
Immunogen
Species (Isotype) human (IgG1λ)
Ab Type cluster II
Research Contact R. A. Myers State of Maryland Dept. of Health
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996; Chen *et al.* 1995; Myers *et al.* 1993
Keywords antibody binding site definition and exposure, review

- Md-1: NIH AIDS Research and Reference Reagent Program: 1223.
- Md-1: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Md-1: Discontinuous epitope recognizing residues between 563-672, does not recognize cluster I disulfide bridge region – reacts almost exclusively with trimers and tetramers on WB – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding. Binley *et al.* [1996] (**antibody binding site definition and exposure**)
- Md-1: Called MD-1 – one of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation. Chen *et al.* [1995] (**antibody binding site definition and exposure**)
- Md-1: Called MD-1 – discontinuous epitope that binds in the N-terminal region – reacts exclusively with oligomer. Myers *et al.* [1993] (**antibody binding site definition and exposure**)

No. 1193
MAb ID Fab A9 (A9)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster III
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab A9: Called A9. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab A9: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 1194
MAb ID Fab G15 (G15)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster III
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab G15: Called G15. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab G15: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 1195
MAb ID Fab G5
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster III
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab G5: Called G5. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab G5: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 1196
MAb ID Fab L1 (L1)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster III
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996

Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab L1: Called L1. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab L1: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 1197
MAb ID Fab L11 (L11)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster III
References Gorny & Zolla-Pazner 2004; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab L11: Called L11. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab L11: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 1198
MAb ID Fab L2 (L2)
HXB2 Location Env
Author Location gp41 (LAI)
Epitope
Subtype B
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgG1κ)
Ab Type cluster III
Research Contact P. Perrin and D. Burton (Scripps Research Institute, La Jolla, California
References Gorny & Zolla-Pazner 2004; Earl *et al.* 1997; Binley *et al.* 1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review

- Fab L2: Called L2. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- Fab L2: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. Binley *et al.* [1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No. 1199
MAb ID 1281 (1281-D)
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgG1λ)
Ab Type cluster II, six-helix bundle
Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny & Zolla-Pazner 2004; Follis *et al.* 2002; Golding *et al.* 2002b; Verrier *et al.* 2001; Gorny *et al.* 2000; Gorny & Zolla-Pazner 2000; Hioe *et al.* 1997b
Keywords antibody binding site definition and exposure, antibody interactions, review, variant cross-recognition or cross-neutralization

- 1281: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. Gorny & Zolla-Pazner [2004] (**review**)
- 1281: Alanine mutations were introduced into the N- and C-terminal α-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. Follis *et al.* [2002] (**antibody binding site definition and exposure**)
- 1281: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – 98-6 binds to a C-HR hairpin epitope and blocks fusion when added to a 2 hour E/T preincubation at 31.5 C, but if added after 1 hour, doesn't inhibit – this is in contrast to six-helix bundle Abs 167-D and 1281 that inhibit more efficiently when added after one hour of incubation. Golding *et al.* [2002b] (**antibody binding site definition and exposure**)
- 1281: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise

combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. Verrier *et al.* [2001] (**antibody interactions**)
- 1281: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone. Gorny & Zolla-Pazner [2000] (**antibody binding site definition and exposure**)
- 1281: Binds within the region gp41 647-682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. Gorny *et al.* [2000] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 1281: Called 1281-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997b] (**variant cross-recognition or cross-neutralization**)

No. 1200
MAb ID Chessie 8
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing
Immunogen
Species (Isotype) mouse (IgG)
Ab Type cytoplasmic domain
Research Contact G. Lewis
References Smith-Franklin *et al.* 2002; Rovinski *et al.* 1995; Poumbourios *et al.* 1995; Lewis *et al.* 1991

- Chessie 8: This Ab was used in an *in vitro* study demonstrating that HIV-1 antibody and Fcgamma receptors can trap virus on the surface of follicular dendritic cells (FDC)'s and extend the period of infectivity – blocking the FDC-Fcgamma receptor killing the FDC cell reduced their ability to maintain infectivity, and FDC cells seemed to stabilize viral particles and decrease gp120 shedding. Smith-Franklin *et al.* [2002]
- Chessie 8: Used to precipitate gp160 in immunoblots in a study examining the feasibility of using unprocessed gp160 glycoprotein as an immunogen. Rovinski *et al.* [1995]

No. 1201
MAb ID 8F102
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Species (Isotype) mouse (IgG)
Ab Type gp120-CD4 complex
References DeVico *et al.* 1995

- 8F102: MAbs specifically reactive to crosslinked gp120 and CD4 were derived (8F101, 8F102) – conformation dependent – competition studies indicate the epitope is immunogenic in infected humans. DeVico *et al.* [1995]

No. 1202
MAb ID CG-10 (CG10)
HXB2 Location Env
Author Location gp120 (IIIB)
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *Strain:* B clade IIIB *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type gp120-CD4 complex
Research Contact Jonathan Gershoni, Tel Aviv University, Isreal
References Finnegan *et al.* 2001; Oscherwitz *et al.* 1999a; Sullivan *et al.* 1998b; Rizzuto *et al.* 1998; Lee *et al.* 1997; Wu *et al.* 1996; Gershoni *et al.* 1993
Keywords antibody binding site definition and exposure

- CG-10: Called CG10. Using a cell-fusion system, it was found CD4i antibodies 17b, 48d, and CG10 reacted faintly with Env expressing HeLA cells even in the absence of sCD4 or CD4 expressing target cells. Reactivity increased after sCD4 addition, but not after CD4 expressing target cell addition, and binding was not increased at the cell-to-cell CD4-Env interface. This suggests the CD4i co-receptor binding domain is largely blocked at the cell-fusion interface, and so CD4i antibodies would not be able access this site and neutralize cell-mediated viral entry. Finnegan *et al.* [2001] (**antibody binding site definition and exposure**)
- CG-10: Called CG10 – disrupts gp120-CCR5 interaction and competes with MAb 17b –binds near the conserved bridging sheet of gp120 – mutations in positions K/D 121, T/D 123, K/D 207, K/D 421, Q/L 422, Y/S 435, M/A 434, K/A 432 and I/S 423 result in a 70% reduction in CG10 binding. Rizzuto *et al.* [1998]
- CG-10: Called CG10 – CD4BS MAb 15e competes with CG-10 binding, probably due to the disruption of CD4-gp120 by 15e – CD4i MAbs 17b and 48d compete and the binding sites may overlap – MAb A32 enhances binding of 17b, 48d and CG10 – MAbs C11, 2G12 and 212A do not affect CG10 binding – CG-10 can bind gp120 with V1/V2 and V3 deleted – HXBc2 mutations Delta 119-205, 314 G/W, 432 K/A, 183,184 PI/SG decrease CG-10 recognition, HXBc2 mutations Delta 298-327 (V3), 384 Y/E, 298 R/G, 435 Y/S enhance recognition – the CD4 contribution to the CG10 epitope maps to the CD4 CDR2-like loop – CG10 can neutralize HIV-1 in the presence

of sCD4 even though it does not do so in the context of cell surface CD4 binding to gp120. Sullivan *et al.* [1998b]
- CG-10: Called CG10 – Promotes envelope mediated cell fusion between CD4+ cells and cells infected with either T-cell and macrophage tropic viruses – infection of HeLa CD4+ (MAGI) cells by HIV-1 LAI, ELI1, and ELI2 strains was increased two-to four-fold in the presence of CG10. Lee *et al.* [1997]
- CG-10: Called CG10 – MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4, and MAb CG10 does not block this inhibition. Wu *et al.* [1996]
- CG-10: Reacts exclusively with sCD4-gp120 complex, not with sCD4 or gp120 alone. Gershoni *et al.* [1993]

No. 1203
MAb ID CG-25
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type gp120-CD4 complex
References Gershoni *et al.* 1993
- CG-25: Reacts preferentially with sCD4-gp120, also with sCD4, not with gp120. Gershoni *et al.* [1993]

No. 1204
MAb ID CG-4 (CG4)
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing no
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type gp120-CD4 complex
Research Contact Jonathan Gershoni, Tel Aviv University, Isreal
References Gershoni *et al.* 1993
- CG-4: Reacts with gp120 and sCD4-gp120 complex, not with sCD4. Gershoni *et al.* [1993]

No. 1205
MAb ID CG-76
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type gp120-CD4 complex
References Gershoni *et al.* 1993
- CG-76: Reacts equally well with sCD4-gp120 and sCD4, but not with purified gp120. Gershoni *et al.* [1993]

No. 1206
MAb ID CG-9
HXB2 Location Env
Author Location gp120
Epitope
Neutralizing L
Immunogen Vaccine
Vector/Type: sCD4-gp120 complex *HIV component:* gp120
Species (Isotype) mouse (IgG1)
Ab Type gp120-CD4 complex
References Gershoni *et al.* 1993
- CG-9: Reacts preferentially with sCD4-gp120, also with sCD4, not with gp120. Gershoni *et al.* [1993]

No. 1207
MAb ID 105-518
HXB2 Location Env
Author Location gp41 (608–637 HAM112, O group)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* O group HAM112 *HIV component:* gp160
Species (Isotype) mouse (IgG1κ)
Ab Type immunodominant region
References Scheffel *et al.* 1999
- 101-518: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity. Scheffel *et al.* [1999]

No. 1208
MAb ID 31A1
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgMκ/λ)
Ab Type p24+gp41
References Pollock *et al.* 1989
- 31A1: Denatured virus was used for *in vitro* stimulation to generate Abs – Reacts with both p24 and gp41. Pollock *et al.* [1989]

No. 1209
MAb ID 39A64
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgMκ/λ)
Ab Type p24+gp41
References Pollock *et al.* 1989
- 39A64: Denatured virus was used for *in vitro* stimulation to generate Abs – Reacts with both p24 and gp41. Pollock *et al.* [1989]

No. 1210
MAb ID 39B86
HXB2 Location Env

Author Location gp41
Epitope
Neutralizing no
Immunogen in vitro stimulation or selection
Species (Isotype) human (IgMκ/λ)
Ab Type p24+gp41
References Pollock *et al.* 1989

- 39B86: Denatured virus was used for *in vitro* stimulation to generate Abs – Reacts with both p24 and gp41. Pollock *et al.* [1989]

No. 1211
MAb ID 9303
HXB2 Location Env
Author Location gp41
Epitope
Neutralizing no
Immunogen
Species (Isotype) mouse
Ab Type p24+gp41
Research Contact Du Pont
References McDougal *et al.* 1996

No. 1212
MAb ID NC-1
HXB2 Location Env
Author Location gp41 (IIIB)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *Strain:* B clade IIIB
HIV component: gp41
Species (Isotype) mouse (IgG2a)
Ab Type six-helix bundle
Research Contact S. Jiang, New York Blood Center, NY, NY
References de Rosny *et al.* 2004a; de Rosny *et al.* 2004b; Follis *et al.* 2002; Yang *et al.* 2002; Yang *et al.* 2000; Jiang *et al.* 1998
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, inter-clade comparisons, variant cross-recognition or cross-neutralization

- NC-1: The MAb 2F5 binds to the C-heptad and is neutralizing, but the MAb D50 binds to the C-heptad and is not neutralizing. 2F5 binds preferentially to native gp41 prior to receptor activation. Trapped fusion-intermediates suggest 2F5 remains present shortly after gp120 triggering by CD4, but may be lost by the time the six-helix bundle is formed. 2F5 neutralization seems to block a later step of the fusion process, but it does not inhibit binding of NC-1, a MAb specific for the six-helix bundle, so it does not prevent formation of the six-helix bundle. The results are most consistent with 2F5 inhibiting a post-fusion-intermediate step. de Rosny *et al.* [2004b] (**antibody binding site definition and exposure**, **antibody interactions**)
- NC-1: The mechanism of 2F5 neutralization was explored, and experiments suggest it is due to interference with a late step in viral entry. 2F5 does not block six-helix bundle formation, as 2F5 prebinding does not inhibit NC-1 binding, a MAb that binds specifically to the six-helix bundle. de Rosny *et al.* [2004a] (**antibody binding site definition and exposure**)
- NC-1: Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. Follis *et al.* [2002] (**antibody binding site definition and exposure**)
- NC-1: Uncleaved soluble gp140 can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif (gp140delta683(-/GCN4)) or using a T4 trimeric motif derived from T4 bacteriophage fibritin (gp140delta683(-/FT)) – NC-1 binds to 15% of the GCN4 motif trimers, but this was significantly reduced for the T4 fibritin stabilized structures, indicating little is in the six-helix bundle, fusogenic conformation. Yang *et al.* [2002] (**antibody binding site definition and exposure**)
- NC-1: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – approximately 16% of the gp140(-GNC4) stabilized trimer recognized by pooled sera was precipitated by NC-1, indicating that at a fraction assumes a fusogenic gp41 six-helix bundle conformation – gp140(-) monomers were not able to bind to the NC-1, nor was gp130(-/GCN4) glycoprotein, consistent with the expectation that the absence of C34 helices would preclude formation of the six-helix bundle. Yang *et al.* [2000] (**antibody binding site definition and exposure**)
- NC-1: Ab elicited in response to immunization with N36(L6)C34, a peptide that folds into a six helix bundle like gp41 – NC-1 binds to the surface of HIV-1 infected cells only in the presence of sCD4, recognizing the fusogenic core structure – binding affinity was decreased by point mutations that disrupt core formation and abolish membrane fusion activity, (I573P and I573A) – NC-1 can recognize discontinuous epitopes from B clade isolate SC, but not E clade strain N243, O group strain GAB, or HIV-2 ROD. Jiang *et al.* [1998] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

IV-C-17 Nef Antibodies

No. 1213
MAb ID 4H4
HXB2 Location Nef (1–33)
Author Location Nef (1–33 IIIB)
Epitope MGGKWSKSSVVGWPTVRERMRRAPTVRERMRR-AEPAADGVGAA
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade IIIB
HIV component: Nef

Species (Isotype) human (IgG1)
References Otake *et al.* 1994

- 4H4: This MAb, elicited by vaccination with a Nef fusion protein, could not detect Nef protein on the cell surface – C-term anti-Nef Abs could. Otake *et al.* [1994]

No. 1214
MAb ID polyclonal
HXB2 Location Nef (9–24)
Author Location Nef (9–24)
Epitope SVIGWLTVRERMRRAE
Neutralizing no
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade BRU *HIV component:* Nef
Species (Isotype) mouse (IgG)
References Tahtinen *et al.* 2001

- BALB/c mice were immunized with a pBN-vector expressing HIV-1 nef, rev, or tat genes – DNA loaded onto gold microparticles was delivered using a gene gun, and DNA dissolved in saline was given intradermally or intramuscularly – Nef gene gun immunized mice showed the strongest and most long-lasting (6 months) Ab, CTL and proliferative responses – the highest IgG1/IgG2a ratio was observed in the gene gun immunized mice – three Ab binding sites were found in Nef using peptide mapping, although some sera reacted only to complete Nef – Rev- or-Tat immunized mice did not generate an Ab response. Tahtinen *et al.* [2001]

No. 1215
MAb ID 13/042
HXB2 Location Nef (11–20)
Author Location Nef (11–24 BH10)
Epitope VGWPTVRERM
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse
References Schneider *et al.* 1991

- 13/042: Epitope mapped by overlapping decapeptides – core: TVRERM. Schneider *et al.* [1991]

No. 1216
MAb ID 13/035
HXB2 Location Nef (15–24)
Author Location Nef (11–24 BH10)
Epitope TVRERMRRAE
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse
References Schneider *et al.* 1991

- 13/035: Epitope mapped by overlapping decapeptides – core: TVRERM. Schneider *et al.* [1991]

No. 1217
MAb ID A6
HXB2 Location Nef (18–26)
Author Location Nef (18–26 NL-432)
Epitope ERMRRAEPA?
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgM)
References Otake *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation

- A6: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. A6 bound to the peptide spanning amino acids 18-26; we inferred the amino acids from the positions in the NL-43 strain. A6 also bound to the complete Nef protein. Otake *et al.* [1997] (**antibody binding site definition and exposure**, **antibody generation**)

No. 1218
MAb ID AM5C6
HXB2 Location Nef (28–43)
Author Location Nef (28–43 BH10)
Epitope DGVGAASRDLEKHGAI+KAAVDLSHFLK
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse
References Maksiutov *et al.* 2002; Schneider *et al.* 1991

- AM5C6: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. Maksiutov *et al.* [2002]
- AM5C6: Epitope mapped by overlapping decapeptides – core: SRDL – also reacts with Nef(78-92) Schneider *et al.* [1991]

No. 1219
MAb ID AM5C6
HXB2 Location Nef (28–43)
Author Location Nef (28–43 BH10)
Epitope DGVGAASRDLEKHGAI+KAAVDLSHFLK
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse
References Maksiutov *et al.* 2002; Schneider *et al.* 1991

- AM5C6: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. Maksiutov *et al.* [2002]
- AM5C6: Epitope mapped by overlapping decapeptides – core: KAAVDL – also reacts with Nef(28-43) Schneider *et al.* [1991]

No. 1220
MAb ID A7
HXB2 Location Nef (28–45)
Author Location Nef (28–45 NL-432)
Epitope DGVGAVSRDLEKHGAITS?
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG1)

References Otake *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation

- A7: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. A7 bound to the peptide spanning amino acids 28-45; we inferred the amino acids from the positions in the NL-43 strain. A7 did not bind to the complete Nef protein. Otake *et al.* [1997] (**antibody binding site definition and exposure**, **antibody generation**)

No. 1221
MAb ID 25/03
HXB2 Location Nef (30–43)
Author Location Nef (30–43 BH10)
Epitope VGAASRDLEKHGAI
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse
References Maksiutov *et al.* 2002; Schneider *et al.* 1991

- 25/03: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. Maksiutov *et al.* [2002]
- 25/03: Epitope mapped by overlapping decapeptides – core: ASRDLEK. Schneider *et al.* [1991]

No. 1222
MAb ID 26/76
HXB2 Location Nef (30–43)
Author Location Nef (30–43 BH10)
Epitope VGAASRDLEKHGAI
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse
References Maksiutov *et al.* 2002; Schneider *et al.* 1991

- 26/76: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. Maksiutov *et al.* [2002]
- 26/76: Epitope mapped by overlapping decapeptides – core: SRDLEK. Schneider *et al.* [1991]

No. 1223
MAb ID 3F2
HXB2 Location Nef (31–40)
Author Location Nef (31–40 BRU)
Epitope GAASRDLEKH
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Nef
Species (Isotype) mouse (IgG1)
References Maksiutov *et al.* 2002; Ranki *et al.* 1995; Saito *et al.* 1994; Ovod *et al.* 1992

- 3F2: UK Medical Research Council AIDS reagent: EVA3067.1.
- 3F2: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. Maksiutov *et al.* [2002]
- 3F2: Faintly cross-reactive with astrocytes of uninfected control samples. Ranki *et al.* [1995]
- 3F2: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) Ovod *et al.* [1992]

No. 1224
MAb ID 3D12
HXB2 Location Nef (31–50)
Author Location Nef (31–50 BRU)
Epitope GAASRDLEKHGAITSSNTAA
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Nef
Species (Isotype) mouse (IgG1)
References Maksiutov *et al.* 2002; Ranki *et al.* 1995; Saito *et al.* 1994; Ovod *et al.* 1992

- 3D12: There is an anti-RT MAb that also has this name (see.
- 3D12: UK Medical Research Council AIDS reagent: EVA3067.2.
- 3D12: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. Maksiutov *et al.* [2002]
- 3D12: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia. Ranki *et al.* [1995]
- 3D12: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissues. Saito *et al.* [1994]
- 3D12: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) Ovod *et al.* [1992]

No. 1225
MAb ID polyclonal
HXB2 Location Nef (33–65)
Author Location Nef (32–64 LAI, BRU)
Epitope ASRDLEKHGAITSSNTAATNAACAWLEAQEEEE
Subtype B
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein, PLG microparticle *Strain:* B clade BRU, B clade LAI *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA), PLG
Species (Isotype) mouse (IgG1)
References Maksiutov *et al.* 2002; Moureau *et al.* 2002

- This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. Maksiutov *et al.* [2002]
- Nef encapsulated in poly(DL-lactide-co-glycolide) (PLG) had a more prolonged Ab response than Nef in PBS or in Freund's adjuvant (CFA), still strong after 7 months – the response was predominantly IgG1, a Th2 immune response – three linear epitopes, Nef 32-64, 118-167, and 185-205, were frequently recognized by the sera of mice immunized with NefPLG or Nef-CFA, but not after immunization with Nef in PBS, which seemed to preferentially stimulate an Ab response to conformational epitopes. Moureau *et al.* [2002]

No. 1226

MAb ID polyclonal
HXB2 Location Nef (49–64)
Author Location Nef (49–64)
Epitope AATNAACAWLEAQEEE
Neutralizing no
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade BRU *HIV component:* Nef
Species (Isotype) mouse (IgG)
References Tahtinen *et al.* 2001

- BALB/c mice were immunized with a pBN-vector expressing HIV-1 nef, rev, or tat genes – DNA loaded onto gold microparticles was delivered using a gene gun, and DNA dissolved in saline was given intradermally or intramuscularly – Nef gene gun immunized mice showed the strongest and most long-lasting (6 months) Ab, CTL and proliferative responses – the highest IgG1/IgG2a ratio was observed in the gene gun immunized mice – three Ab binding sites were found in Nef using peptide mapping, although some sera reacted only to complete Nef – Rev- or-Tat immunized mice did not generate an Ab response. Tahtinen *et al.* [2001]

No. 1227
MAb ID 3G12
HXB2 Location Nef (51–71)
Author Location Nef (51–71 BRU)
Epitope TNAACAWLEAQEEEEVGFPVT
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Nef
Species (Isotype) mouse (IgG2a)
References Ovod *et al.* 1992

- 3G12: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) Ovod *et al.* [1992]

No. 1228
MAb ID 13/058
HXB2 Location Nef (60–73)
Author Location Nef (60–73 BH10)
Epitope AQEEEEVGFPVTPQ
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse
References Schneider *et al.* 1991

- 13/058: Epitope mapped by overlapping decapeptides – core: EEVGFP. Schneider *et al.* [1991]

No. 1229
MAb ID 26/028
HXB2 Location Nef (60–73)
Author Location Nef (60–73 BH10)
Epitope AQEEEEVGFPVTPQ
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse
References Schneider *et al.* 1991

- 26/028: Epitope mapped by overlapping decapeptides – core: EEVGFPV. Schneider *et al.* [1991]

No. 1230
MAb ID 2E3
HXB2 Location Nef (61–80)
Author Location Nef (61–80 BRU)
Epitope QEEEEVGFPVTPQVPLRPMT
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU *HIV component:* Nef
Species (Isotype) mouse (IgG1)
References Nilsen *et al.* 1996; Ovod *et al.* 1992

- 2E3: There are two MAbs with the name 2E3 – the other one binds to integrase. Nilsen *et al.* [1996]
- 2E3: Two isomorphic forms of Nef were identified, 2E3 reacted with the p24 but not p27 form, and was strain specific (MN and BRU reactive, not IIIB or RF) Ovod *et al.* [1992]

No. 1231
MAb ID polyclonal
HXB2 Location Nef (66–97)
Author Location Nef (66–97 LAI)
Epitope VGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGL
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Nef *Adjuvant:* QS21
Species (Isotype) human (IgG)
References Pialoux *et al.* 2001

- 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 10/28, proliferative in 11/14, and CTL in 13/24 (54%) of testable volunteers – 10/28 had Ab responses to this peptide (N1), 11/24 had proliferative responses, and CTL responses were detected. Pialoux *et al.* [2001]

No. 1232
MAb ID F14.11
HXB2 Location Nef (83–88)
Author Location Nef (83–88)
Epitope AAVDLS
Neutralizing
Immunogen Vaccine
Vector/Type: peptide *HIV component:* Nef
Species (Isotype) mouse (IgG2aκ)
References Chang *et al.* 1998; De Santis *et al.* 1991

- F14.11: Used as a control in a study of Nef-specific single chain Abs constructed from AG11 and EH1. Chang *et al.* [1998]
- F14.11: The MAb was made to a six aa region of Nef that is similar to a region found in thymosin alpha 1 protein – the MAb binds to the natural Nef protein. De Santis *et al.* [1991]

No. 1233
MAb ID 31/03
HXB2 Location Nef (83–103)

Author Location Nef (82–103 BH10)
Epitope AAVDLSHFLKEKGGLEGLIHS
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse
References Schneider *et al.* 1991

- 31/03: Epitope mapped by overlapping decapeptides – mapping suggests complex epitope in this region. Schneider *et al.* [1991]

No. 1234
MAb ID F4
HXB2 Location Nef (115–126)
Author Location Nef (115–126 NL-432)
Epitope YHTQGYFPDWQN?
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* Nef
Species (Isotype) mouse (IgG1)
References Otake *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation

- F4: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. F4 bound to the peptide spanning amino acids 115-126; we inferred the amino acids from the positions in the NL-43 strain. A6 also bound to the complete Nef protein. Otake *et al.* [1997] (**antibody binding site definition and exposure**, **antibody generation**)

No. 1235
MAb ID F2
HXB2 Location Nef (115–136)
Author Location Nef (115–137 NL-432)
Epitope YHTQGYFPDWQNYTPGPGVRYP?
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG1)
References Otake *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation

- F2: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. F2 bound to the peptide spanning amino acids 115-137; we inferred the amino acids from the positions in the NL-43 strain. F2 also bound to the complete Nef protein. Otake *et al.* [1997] (**antibody binding site definition and exposure**, **antibody generation**)

No. 1236
MAb ID polyclonal
HXB2 Location Nef (117–147)
Author Location Nef (117–147 LAI)
Epitope TQGYFPDWQNYTPGPGVRYPLTFGWCYKLVP
Subtype B
Neutralizing no
Immunogen Vaccine
Vector/Type: lipopeptide *Strain:* B clade LAI *HIV component:* Nef *Adjuvant:* QS21
Species (Isotype) human (IgG)
References Pialoux *et al.* 2001

- 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28, proliferative in 3/24, and CTL in 13/24 (54%) of testable volunteers – 20/28 had antibody responses to this particular peptide (N2), 3/24 had proliferative responses, and CTL responses were detected. Pialoux *et al.* [2001]

No. 1237
MAb ID polyclonal
HXB2 Location Nef (118–133)
Author Location Nef (118–133)
Epitope QGYFPDWQNYTPGPGV
Neutralizing no
Immunogen Vaccine
Vector/Type: DNA *Strain:* B clade BRU *HIV component:* Nef
Species (Isotype) mouse (IgG)
References Tahtinen *et al.* 2001

- BALB/c mice were immunized with a pBN-vector expressing HIV-1 nef, rev, or tat genes—DNA loaded onto gold microparticles was delivered using a gene gun, and DNA dissolved in saline was given intradermally or intramuscularly—Nef gene gun immunized mice showed the strongest and most long-lasting (6 months) Ab, CTL and proliferative responses—the highest IgG1/IgG2a ratio was observed in the gene gun immunized mice—three Ab binding sites were found in Nef using peptide mapping, although some sera reacted only to complete Nef—Rev- or Tat-immunized mice did not generate an Ab response. Tahtinen *et al.* [2001]

No. 1238
MAb ID polyclonal
HXB2 Location Nef (119–168)
Author Location Nef (118–167 LAI, BRU)
Epitope GYFPDWQNYTPGPGVRYPLTFGWCYKLVPVEP-DKVEEANKGENTSLLHPV
Subtype B
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein, PLG microparticle *Strain:* B clade BRU, B clade LAI *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA), PLG
Species (Isotype) mouse (IgG1)
References Maksiutov *et al.* 2002; Moureau *et al.* 2002

- This epitope is similar to a fragment of the human protein Bone-derived growth factor, PLEPAKLEE, and to Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG. Maksiutov *et al.* [2002]
- Nef encapsulated in poly(DL-lactide-co-glycolide) (PLG) had a more prolonged Ab response than Nef in PBS or in Freund's adjuvant (CFA), still strong after 7 months – the response was predominantly IgG1, a Th2 immune response – three linear

epitopes, Nef 32-64, 118-167, and 185-205, were frequently recognized by the sera of mice immunized with NefPLG or Nef-CFA, but not after immunization with Nef in PBS, which seemed to preferentially stimulate an Ab response to conformational epitopes. Moureau *et al.* [2002]

No. 1239
MAb ID F3
HXB2 Location Nef (128–137)
Author Location Nef (128–137 NL-432)
Epitope TPGPGVRYPL?
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgG1)
References Kawai *et al.* 2003; Otake *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation, complement

- F3: Used as a control for Nef binding in a study designed to elicit anti-Nef IgM human Abs in trans-chromosome mice that carry human chromosomes responsible for Ig production. These mice were immunized with recombinant Nef protein. Human heavy chain, mouse light chain anti-Nef IgM were obtained. The hope was that these human IgM anti-Nef chimeric Abs would activate complement mediated cytolysis; C3 deposition was induced but not at high enough levels to induce lysis. Kawai *et al.* [2003] (**complement**)
- F3: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. F3 bound to the peptide spanning amino acids 128-137; we inferred the amino acids from the positions in the NL-43 strain. F3 also bound to the complete Nef protein. Otake *et al.* [1997] (**antibody binding site definition and exposure**, **antibody generation**)

No. 1240
MAb ID F8
HXB2 Location Nef (128–137)
Author Location Nef (128–137 NL-432)
Epitope TPGPGVRYPL?
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgM)
References Otake *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation

- F8: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. F8 bound to the peptide spanning amino acids 128-137; we inferred the amino acids from the positions in the NL-43 strain. F8 also bound to the complete Nef protein. Otake *et al.* [1997] (**antibody binding site definition and exposure**, **antibody generation**)

No. 1241
MAb ID F1
HXB2 Location Nef (148–157)
Author Location Nef (148–157 IIIB)
Epitope VEPDKVEEAN
Neutralizing
Immunogen
Species (Isotype) mouse (IgM)
References Fujii *et al.* 1996b; Fujii *et al.* 1996c; Otake *et al.* 1994; Fujii *et al.* 1993

- F1: Insect cells expressing myristylated Nef proteins on their cell surface can induce cytolysis of unstimulated CD4+ cells – this response is not due to MHC restricted CTL activity – the cell surface of Nef expressing insect cells carry Nef that can be recognized by MAbs E7 and E9 but not F1. Fujii *et al.* [1996c]
- F1: A carboxy-terminal domain of Nef on the cell surface induces cytolysis of CD4+ T cells. Fujii *et al.* [1996b]
- F1: The C-term end of Nef is accessible to Abs at the cell surface – stained IIIB/M10, but not MN/M10, cells. Fujii *et al.* [1993]; Otake *et al.* [1994]

No. 1242
MAb ID 2F2
HXB2 Location Nef (151–170)
Author Location Nef (151–170 BRU)
Epitope DKVEEANKGENTSLLHPVSL
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse (IgG1)
References Maksiutov *et al.* 2002; Ranki *et al.* 1995; Saito *et al.* 1994; Ovod *et al.* 1992

- 2F2: UK Medical Research Council AIDS reagent: EVA3067.3.
- 2F2: This epitope is similar to a fragment of the human protein Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG. Maksiutov *et al.* [2002]
- 2F2: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia. Ranki *et al.* [1995]
- 2F2: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissue. Saito *et al.* [1994]
- 2F2: Strain specific (MN and BRU reactive, not IIIB or RF) Ovod *et al.* [1992]

No. 1243
MAb ID E9
HXB2 Location Nef (158–181)
Author Location Nef (158–206 IIIB)
Epitope KGENTSLLHPVSLHGMDDPEREVL
Neutralizing
Immunogen
Species (Isotype) mouse (IgM)
References Maksiutov *et al.* 2002; Fujii *et al.* 1996b; Fujii *et al.* 1996c; Otake *et al.* 1994; Fujii *et al.* 1993

- E9: This epitope is similar to a fragment of the human protein Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG. Maksiutov *et al.* [2002]
- E9: A carboxy-terminal domain of Nef on the cell surface induces cytolysis of CD4+ T cells. Fujii *et al.* [1996b]

- E9: Insect cells expressing myristylated Nef proteins on their cell surface can induce cytolysis of unstimulated CD4+ cells – this response is not due to MHC restricted CTL activity – the cell surface of Nef expressing insect cells carry Nef that can be recognized by MAbs E7 and E9 but not F1. Fujii *et al.* [1996c]
- E9: The C-term end of Nef is accessible to Abs at the cell surface – stained IIIB/M10, but not MN/M10, cells. Fujii *et al.* [1993]; Otake *et al.* [1994]

No. 1244
MAb ID 3E6
HXB2 Location Nef (161–180)
Author Location Nef (161–180 BRU)
Epitope NTSLLHPVSLHGMDDPEREV
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: Nef
Species (Isotype) mouse (IgG1)
References Maksiutov *et al.* 2002; Ranki *et al.* 1995; Saito *et al.* 1994; Ovod *et al.* 1992

- 3E6: UK Medical Research Council AIDS reagent: EVA3067.4.
- 3E6: This epitope is similar to a fragment of the human protein Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG. Maksiutov *et al.* [2002]
- 3E6: Faintly cross-reactive with astrocytes of uninfected control samples. Ranki *et al.* [1995]
- 3E6: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) Ovod *et al.* [1992]

No. 1245
MAb ID E5
HXB2 Location Nef (170–181)
Author Location Nef (170–181)
Epitope LHGMDDPEREVL?
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade NL43
HIV component: Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Species (Isotype) mouse (IgM)
References Otake *et al.* 1997
Keywords antibody binding site definition and exposure, antibody generation

- E5: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. E5 bound to the peptide spanning amino acids 170-181; we inferred the amino acids from the positions in the NL-43 strain. E5 also bound to the complete Nef protein. Otake *et al.* [1997] (**antibody binding site definition and exposure**, **antibody generation**)

No. 1246
MAb ID 2A3
HXB2 Location Nef (171–190)
Author Location Nef (171–190 BRU)
Epitope HGMDDPEREVLEWRFDSRLA
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: Nef
Species (Isotype) mouse (IgG1)
References Ovod *et al.* 1992

- 2A3: Reacted with Nef from different HIV-1 strains (BRU, IIIB, MN, but not RF) Ovod *et al.* [1992]

No. 1247
MAb ID 2E4
HXB2 Location Nef (171–190)
Author Location Nef (171–190 BRU)
Epitope HGMDDPEREVLEWRFDSRLA
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: Nef
Species (Isotype) mouse (IgG1)
References Ovod *et al.* 1992

- 2EA: Reacted with Nef from different HIV-1 strains (BRU, IIIB, MN but not RF) Ovod *et al.* [1992]

No. 1248
MAb ID 2H12
HXB2 Location Nef (171–190)
Author Location Nef (171–190 BRU)
Epitope HGMDDPEREVLEWRFDSRLA
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: Nef
Species (Isotype) mouse (IgG1)
References Ranki *et al.* 1995; Saito *et al.* 1994; Ovod *et al.* 1992

- 2H12: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia. Ranki *et al.* [1995]
- 2H12: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissue. Saito *et al.* [1994]
- 2H12: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) Ovod *et al.* [1992]

No. 1249
MAb ID 3A2
HXB2 Location Nef (171–190)
Author Location Nef (171–190 BRU)
Epitope HGMDDPEREVLEWRFDSRLA
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BRU
HIV component: Nef
Species (Isotype) mouse (IgG1)
References Ranki *et al.* 1995; Saito *et al.* 1994; Ovod *et al.* 1992

- 3A2: UK Medical Research Council AIDS reagent: EVA3067.5.
- 3A2: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia. Ranki *et al.* [1995]

- 3A2: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissue. Saito *et al.* [1994]
- 3A2: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) Ovod *et al.* [1992]

No. 1250
MAb ID NF1A1
HXB2 Location Nef (173–206)
Author Location Nef (173–206)
Epitope MDDPEREVLEWRFDSRLAFHHVARELHPEYFK-NC
Neutralizing
Immunogen
Species (Isotype) mouse
References Kaminchik *et al.* 1990

- NF1A1: Recognizes the Nef protein of the two isolates BH10 and LAV1 – low affinity. Kaminchik *et al.* [1990]

No. 1251
MAb ID polyclonal
HXB2 Location Nef (186–206)
Author Location Nef (185–205 LAI, BRU)
Epitope DSRLAFHHVARELHPEYFKNC
Subtype B
Neutralizing
Immunogen HIV-1 infection, Vaccine
Vector/Type: protein, PLG microparticle *Strain:* B clade BRU, B clade LAI *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA), PLG
Species (Isotype) mouse (IgG1)
References Moureau *et al.* 2002

- Nef encapsulated in poly(DL-lactide-co-glycolide) (PLG) had a more prolonged Ab response than Nef in PBS or in Freund's adjuvant (CFA), still strong after 7 months – the response was predominantly IgG1, a Th2 immune response – three linear epitopes, Nef 32-64, 118-167, and 185-205, were frequently recognized by the sera of mice immunized with NefPLG or Nef-CFA, but not after immunization with Nef in PBS, which seemed to preferentially stimulate an Ab response to conformational epitopes. Moureau *et al.* [2002]

No. 1252
MAb ID E7
HXB2 Location Nef (192–206)
Author Location Nef (192–206 IIIB)
Epitope HHVARELHPEYFKNC
Neutralizing
Immunogen
Species (Isotype) mouse (IgM)
References Fujii *et al.* 1996d; Fujii *et al.* 1996b; Fujii *et al.* 1996a; Fujii *et al.* 1996c; Otake *et al.* 1994; Fujii *et al.* 1993

- E7: Insect cells expressing myristylated Nef proteins on their cell surface can induce cytolysis of unstimulated CD4+ cells – this response is not due to MHC restricted CTL activity – the cell surface of Nef expressing insect cells carry Nef that can be recognized by MAbs E7 and E9 but not F1. Fujii *et al.* [1996c]
- E7: Nef forms a homomeric oligomerizing structure, and using E7 and membrane immunofluorescence or immunoelectron microscopy, was shown to clusters on the surface of HIV-1 infected CD4+ cells. Fujii *et al.* [1996a]
- E7: A carboxy-terminal domain of Nef on the cell surface induces cytolysis of CD4+ T cells. Fujii *et al.* [1996b]
- E7: Soluble Nef inhibits proliferation of CD4+ cells, and Nef cross-linking by MAbs may induce anti-CD4 cytocidal activity – sera from HIV+ individuals contain soluble Nef, thus this may be important for immune dysfunction and disease progression. Fujii *et al.* [1996d]
- E7: The C-term end of Nef is accessible to Abs at the cell surface – stained IIIB/M10, but not MN/M10, cells. Fujii *et al.* [1993]; Otake *et al.* [1994]

No. 1253
MAb ID AE6
HXB2 Location Nef (194–206)
Author Location Nef (LAI)
Epitope VARELHPEYFKNC
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse (IgG1κ)
Ab Type C-term
Research Contact Frank Jirik, Centre for Molecular Med and Therapeutics, U. B. C., Vancouver, B. C. Canada
References Chang *et al.* 1998

- AE6: The light and heavy chains of three MAbs (AG11, AE6, EH1) specific to C-terminus of NEF were cloned and variable regions sequenced – the complementarity determining regions (CDR) of AG11 and AE6 were highly related (95.1% at the DNA level) and bound LAI Nef, but not SF2 Nef – EH1 bound to SF2 and LAI and cross-competed AG11 and AE6 but had a distinctive CDR (57.9% similar to AG11) – single chain Abs were constructed from AG11 and EH1. Chang *et al.* [1998]

No. 1254
MAb ID AG11
HXB2 Location Nef (194–206)
Author Location Nef (LAI)
Epitope VARELHPEYFKNC
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse (IgG1κ)
Ab Type C-term
Research Contact Frank Jirik, Centre for Molecular Med and Therapeutics, U. B. C., Vancouver, B. C. Canada
References Chang *et al.* 1998

- AG11: The light and heavy chains of three MAbs (AG11, AE6, EH1) specific to C-terminus of NEF were cloned and variable regions sequenced – the complementarity determining regions (CDR) of AG11 and AE6 were highly related (95.1% at the DNA level) and bound LAI Nef, but not SF2 Nef – EH1 bound to SF2 and LAI and cross-competed AG11 and AE6 but had a

distinctive CDR (57.9% similar to AG11) – single chain Abs were constructed from AG11 and EH1 and subcloned into a eukaryotic expression vector with a green fluorescent protein marker to allow intracellular expression – the single chain Abs bind Nef intracellularly and may be useful to better understand the role of Nef and as a gene therapy model. Chang *et al.* [1998]

No. 1255
MAb ID EH1
HXB2 Location Nef (194–206)
Author Location Nef (SF2)
Epitope MARELHPEYYKDC
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Species (Isotype) mouse (IgG1κ)
Ab Type C-term
Research Contact Frank Jirik, Centre for Molecular Med and Therapeutics, U. B. C., Vancouver, B. C. Canada
References Chang *et al.* 1998

- EH1: The light and heavy chains of three MAbs (AG11, AE6, EH1) specific to C-terminus of NEF were cloned and variable regions sequenced – the complementarity determining regions (CDR) of AG11 and AE6 were highly related (95.1% at the DNA level) and bound LAI Nef, but not SF2 Nef – EH1 bound to SF2 and LAI and cross-competed AG11 and AE6 but had a distinctive CDR (57.9% similar to AG11) – single chain Abs were constructed from AG11 and EH1 and subcloned into a eukaryotic expression vector with a green fluorescent protein marker to allow intracellular expression – the single chain Abs bind Nef intracellularly and may be useful to better understand the role of Nef and as a gene therapy model. Chang *et al.* [1998]

No. 1256
MAb ID 3B4B
HXB2 Location Nef
Author Location Nef
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Adjuvant: Incomplete Freund's Adjuvant (IFA)
Species (Isotype) transgenic mouse (IgM)
References Kawai *et al.* 2003
Keywords antibody generation, complement

- 3B4B: The goal of this study was to elicit anti-Nef IgM human Abs in trans-chromosome mice that carry human chromosomes responsible for Ig production. These mice were immunized with recombinant Nef protein. Two human heavy chain, mouse light chain anti-Nef IgM were obtained, 3B4B and 3H3E; 3B4B was able to stain MOLT4/IIIB cells with greater intensity. The hope was that these human IgM anti-Nef chimeric Abs would activate complement mediated cytolysis; C3 deposition was induced but not at high enough levels to induce lysis. Kawai *et al.* [2003] (**antibody generation**, **complement**)

No. 1257
MAb ID 3H3E
HXB2 Location Nef
Author Location Nef
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *HIV component:* Nef
Adjuvant: Complete Freund's Adjuvant (CFA)
Species (Isotype) transgenic mouse (IgM)
References Kawai *et al.* 2003
Keywords antibody generation, complement

- 3H3E: The goal of this study was to elicit anti-Nef IgM human Abs in trans-chromosome mice that carry human chromosomes responsible for Ig production. These mice were immunized with recombinant Nef protein. Two human heavy chain, mouse light chain anti-Nef IgM were obtained, 3B4B and 3H3E; 3B4B was able to stain MOLT4/IIIB cells with greater intensity. The hope was that these human IgM anti-Nef chimeric Abs would activate complement mediated cytolysis; C3 deposition was induced but not at high enough levels to induce lysis. Kawai *et al.* [2003] (**antibody generation**, **complement**)

No. 1258
MAb ID 6.1
HXB2 Location Nef
Author Location Nef (JRCSF)
Epitope
Subtype B
Neutralizing
Immunogen
Species (Isotype) mouse
References Ranki *et al.* 1995

- 6.1: Raised against CNS primary isolates, stains astrocytes more densely than other Nef MAbs – Nef expression associated with dementia. Ranki *et al.* [1995]
- 6.1: NIAID Repository number 1123. Ranki *et al.* [1995]

No. 1259
MAb ID NF2B2
HXB2 Location Nef
Author Location Nef (20–78 BH10)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: Nef
Species (Isotype) mouse
References Kaminchik *et al.* 1990

- NF2B2: NIH AIDS Research and Reference Reagent Program: 456.
- NF2B2: Recognizes the Nef protein of the two isolates BH10 and LAV1. Kaminchik *et al.* [1990]

No. 1260
MAb ID NF3A3
HXB2 Location Nef
Author Location Nef (20–78 BH10)
Epitope

Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: Nef
Species (Isotype) mouse
References Kaminchik *et al.* 1990

- NF3A3: Recognizes the Nef protein of the two isolates BH10 and LAV1 – low affinity. Kaminchik *et al.* [1990]

No. 1261
MAb ID NF8B4
HXB2 Location Nef
Author Location Nef (BH10)
Epitope
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade BH10
HIV component: Nef
Species (Isotype) mouse
References Kaminchik *et al.* 1990

- NF8B4: Does not recognize Nef CNBr cleavage products – recognizes intact BH10 Nef but not LAV1 Nef. Kaminchik *et al.* [1990]

No. 1262
MAb ID polyclonal
HXB2 Location Nef
Author Location Nef
Epitope
Subtype B
Neutralizing
Immunogen Vaccine
Vector/Type: protein *Strain:* B clade LAI, SIV *HIV component:* gp120, Nef, Tat *Adjuvant:* AS02A (oil-in-water emulsion, 3D-monophosphoryl lipid A, QS21), AS06 (CpG, aluminum hydroxide)
Species (Isotype) macaque (IgG)
References Voss *et al.* 2003
Keywords adjuvant comparison, variant cross-recognition or cross-neutralization

- Monkeys were immunized with different combinations of gp120/NefTat/SIV-Tat three times over a three-month time period and intravenously challenged with SHIV 89.6P four weeks after the last immunzation. Vaccination induced anti-Tat, -Nef and -gp120 Ab responses that decreased until challenge. Neutralizing Ab responses against HIV-1 MN and HIV-1 W61D were observed. Vaccination with the combination of all three proteins reduced viral load and kept animals from a CD4+ T cell decline, preventing AIDS for more than 2.5 years. The adjuvant AS02A elicited NAbs and protected from disease, while AS06 did not. gp120 alone or TatNef/SIV-Tat without gp120 could not protect from disease. Voss *et al.* [2003] (**adjuvant comparison**, **variant cross-recognition or cross-neutralization**)

No. 1263
MAb ID AE6
HXB2 Location Nef
Author Location Nef
Epitope
Neutralizing
Immunogen
Species (Isotype) mouse
Ab Type C-term
Research Contact James Hoxie, Div of AIDS, NIAID, NIH
References Tornatore *et al.* 1994; Greenway *et al.* 1994

- AE6: NIH AIDS Research and Reference Reagent Program: 709.

IV-C-18 HIV-1 Antibodies

No. 1264
MAb ID
HXB2 Location HIV-1
Author Location
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype)
References Goepfert 2003
Keywords review

- A general review of anti-HIV human immune responses and the implications of these responses for vaccines, summarizing neutralizing antibodies, CD4+ and CD8+ T cell responses. A general overview of methods used to study these responses is presented. Goepfert [2003] (**review**)

No. 1265
MAb ID polyclonal
HXB2 Location HIV-1
Author Location
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Fournier *et al.* 2002b

- Purified B lymphocytes secret only a fraction of Ig and anti-HIV-1 Ab compared with unfractionated cells because monocytes and natural killer cells enhance both secretions by cell-to-cell contacts, involving adhesion and CD27, CD80 costimulatory molecules and IL-6 – cell-to-cell contacts and soluble factors induce maturation of activated B cells *in vitro* to allow prolonged survival and terminal differentiation. Fournier *et al.* [2002b]

No. 1266
MAb ID polyclonal
HXB2 Location HIV-1
Author Location
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Fournier *et al.* 2002a

- An early and sustained fall in plasma viral load to below detection was observed in 17 HAART responders while HIV-1 RNA remained detectable in 13 incomplete responders – HIV-1 specific Ab secretion decreased in parallel with plasma viral load – HIV-1 specific Abs became negative in only six responders, and was correlated with greater increases of CD4 T-cell counts and higher levels of HIV-specific IgA secretion at baseline – persistent immune activation may be due to residual HIV antigen. Fournier *et al.* [2002a]

No. 1267
MAb ID polyclonal
HXB2 Location HIV-1
Author Location
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human
References Subbramanian *et al.* 2002

- Sera from 39 patients were used to study the relative prevalence of neutralizing Abs (NAbs), ADCC-Abs and enhancing Abs – 69% of the sera were positive for NAbs but only 39% could neutralize in the presence of complement – 60% had ADCC Abs – 72% mediated the enhancement of infection in the presence of complement. Subbramanian *et al.* [2002]

No. 1268
MAb ID polyclonal
HXB2 Location HIV-1
Author Location
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgA, IgG1)
References Battle-Miller *et al.* 2002

- In a study of HIV-1 infected women, ADCC Abs were detected in 16% (12/51) of cervicovaginal fluids, and 56% (25/45) of serum samples – 3 women had ADCC in cervical lavage fluids, but not sera, suggesting local production. Battle-Miller *et al.* [2002]

No. 1269
MAb ID polyclonal
HXB2 Location HIV-1
Author Location
Epitope
Neutralizing
Immunogen HIV-1 infection
Species (Isotype) human (IgA1, IgA2, IgM)
References Wu & Jackson 2002

- IgA1 accounted for the majority of anti-HIV-1 IgA in the saliva in HIV-1 infected individuals – there was no anti-gp41 IgA in saliva, in contrast to plasma – lower levels of IgA and IgM were found in saliva than in plasma. Wu & Jackson [2002]

No. 1270
MAb ID polyclonal
HXB2 Location HIV-1
Author Location
Epitope
Subtype B
Neutralizing P
Immunogen HIV-1 infection
Species (Isotype) human
References Hioe *et al.* 1997a

- Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. Hioe *et al.* [1997a]

No. 1271
MAb ID polyclonal
HXB2 Location HIV-1
Author Location
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgA, IgG)
References Oelemann *et al.* 2002

- A urine based commercial EIA kit from Calypte Biomedical Corporation, Berkeley, CA was found to work well as a primary screening for HIV in Brazilian samples – 76 HIV+ samples were correctly identified (100% sensitivity), and 278/284 negative samples 97.9% specificity. Oelemann *et al.* [2002]

No. 1272
MAb ID polyclonal
HXB2 Location HIV-1
Author Location HIV-1
Epitope
Neutralizing no
Immunogen HIV-1 infection
Species (Isotype) human (IgE)
References Pellegrino *et al.* 2002; Secord *et al.* 1996

- Pediatric long term survivors (LTS) have been found to carry HIV-1 specific IgE – serum from these children inhibit HIV-1 production in culture, but this inhibition did not seem to be due to neutralization, rather due to a cytoxic event – serum lost the HIV-1 inhibitory effect when depleted of IgE. Pellegrino *et al.* [2002]
- HIV-specific IgE found in clinically healthy HIV-1 infected children. Secord *et al.* [1996]

No. 1273
MAb ID polyclonal
HXB2 Location HIV-1
Author Location gp120 and p55
Epitope
Neutralizing no
Immunogen Vaccine

Vector/Type: vaccinia *Strain:* B clade 89.6 *HIV component:* Env, Gag-Pol *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)

Species (Isotype) macaque

References Ambrose *et al.* 2003

Keywords genital and mucosal immunity

- Systemic priming with rVVs expressing HIV-1 Env and SHIV Gag-Pol followed by intragastric and intranasal mucosal boosting of LT(R192G) and aldrithiol-2 (AT-2)-inactiviated SHIV induced SHIV-specific IgA and IgG plasma and mucosal Abs. Viral loads in vaccinated animals were reduced after vaginal challenge with SHIV 89.6. Ambrose *et al.* [2003] (**genital and mucosal immunity**)

IV-D

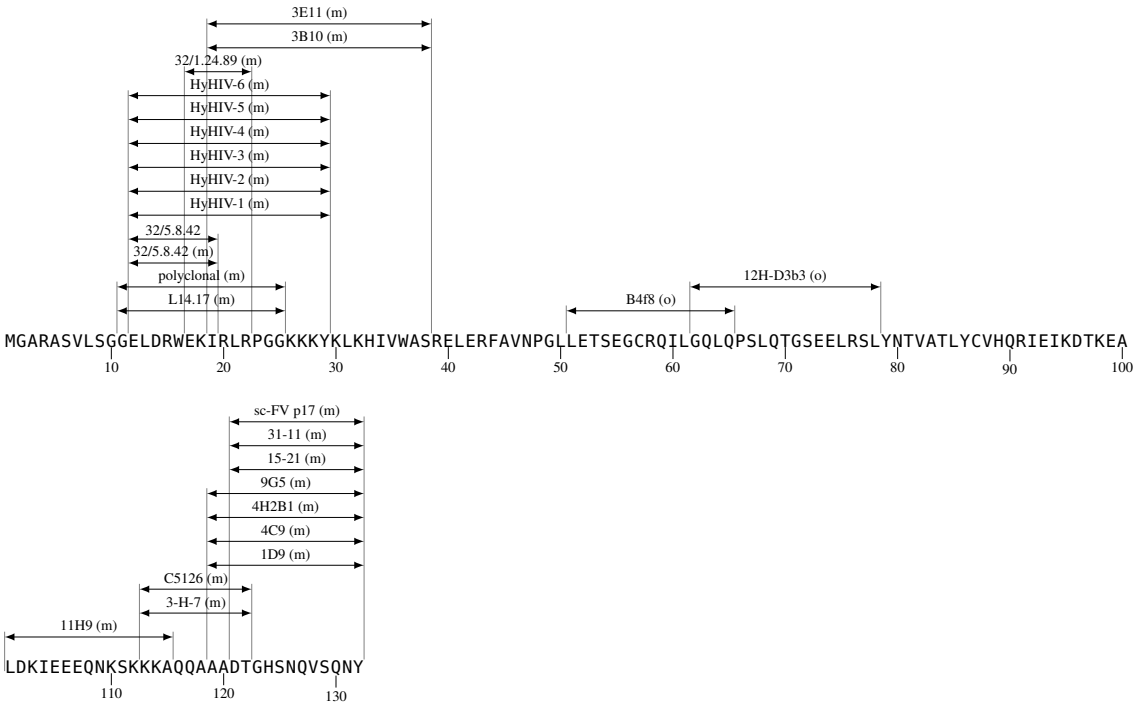
Maps of MAb Locations Plotted by Protein

Linear epitopes less than of 21 amino acids or less are shown with their antibody ID and the experimental species.

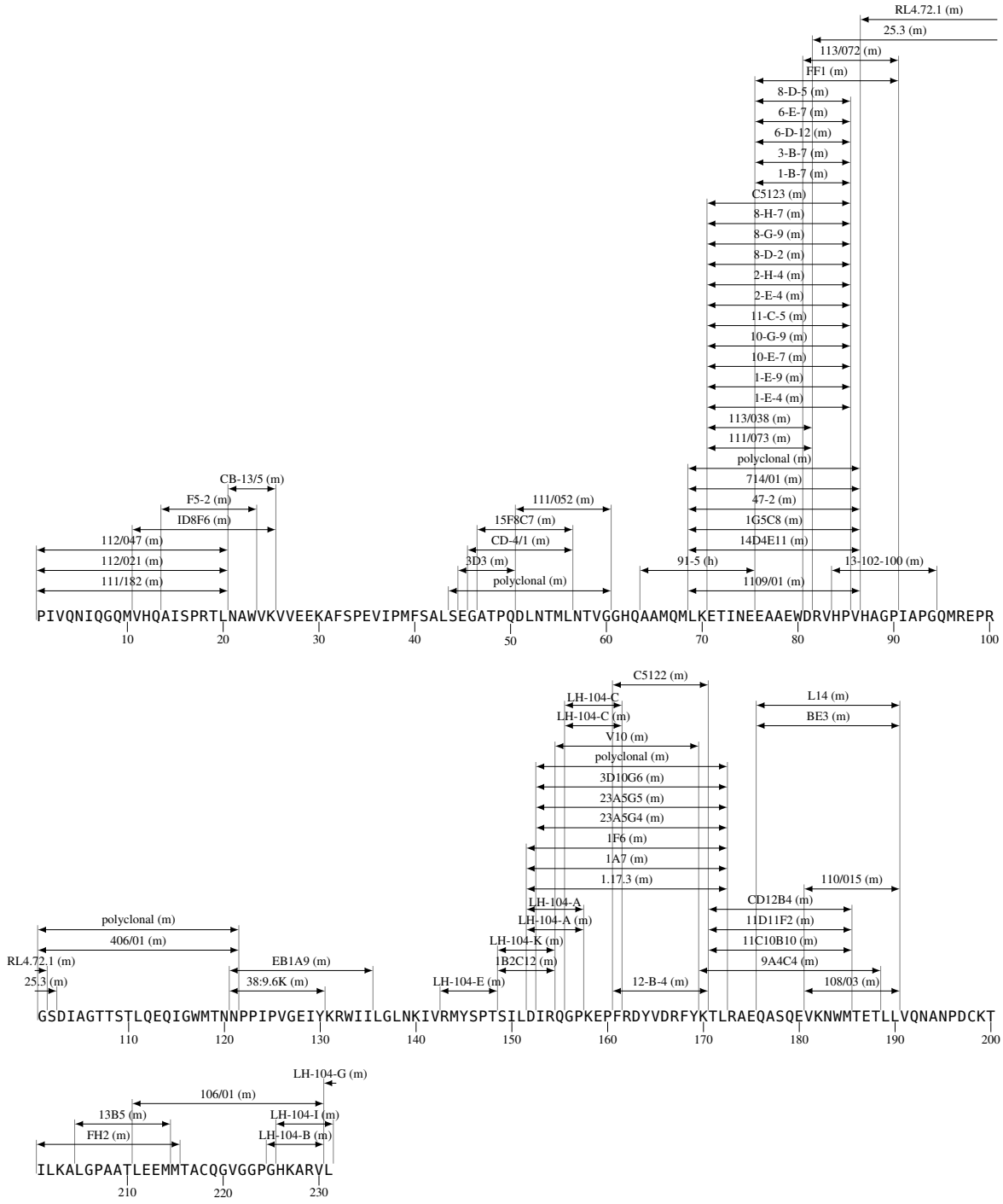
Key	Species
h	human
p	non-human primate
m	murine
o	other

Table IV-D.1: The species that the epitope was generated in and derived from.

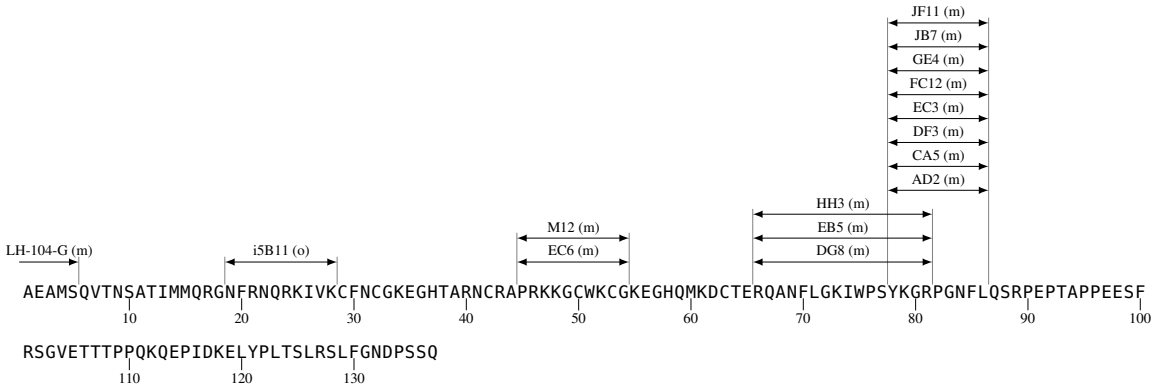
IV-D-1 Gag p17 Ab Epitope Map



IV-D-2 Gag p24 Ab Epitope Map

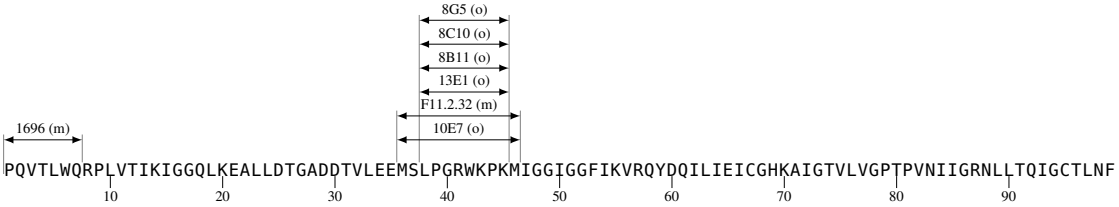


IV-D-3 Gag p2p7p1p6 Ab Epitope Map

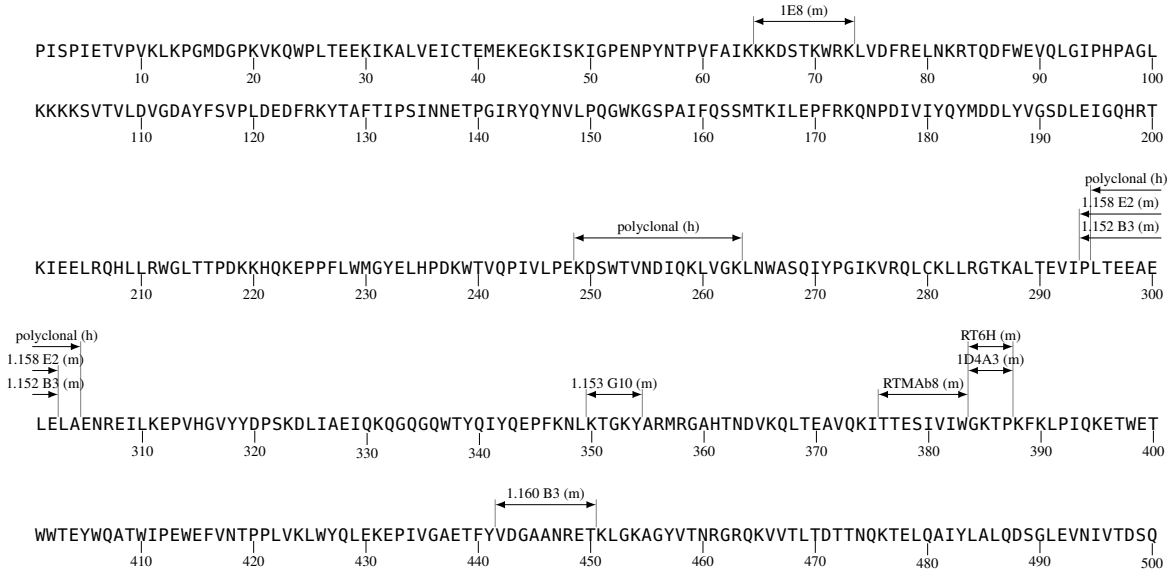


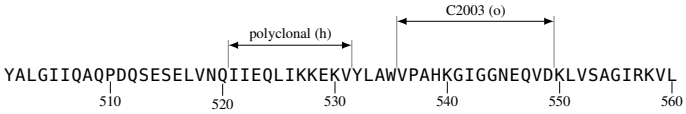
IV-D-4 Gag/Pol TF Ab Epitope Map

IV-D-5 Protease Ab Epitope Map

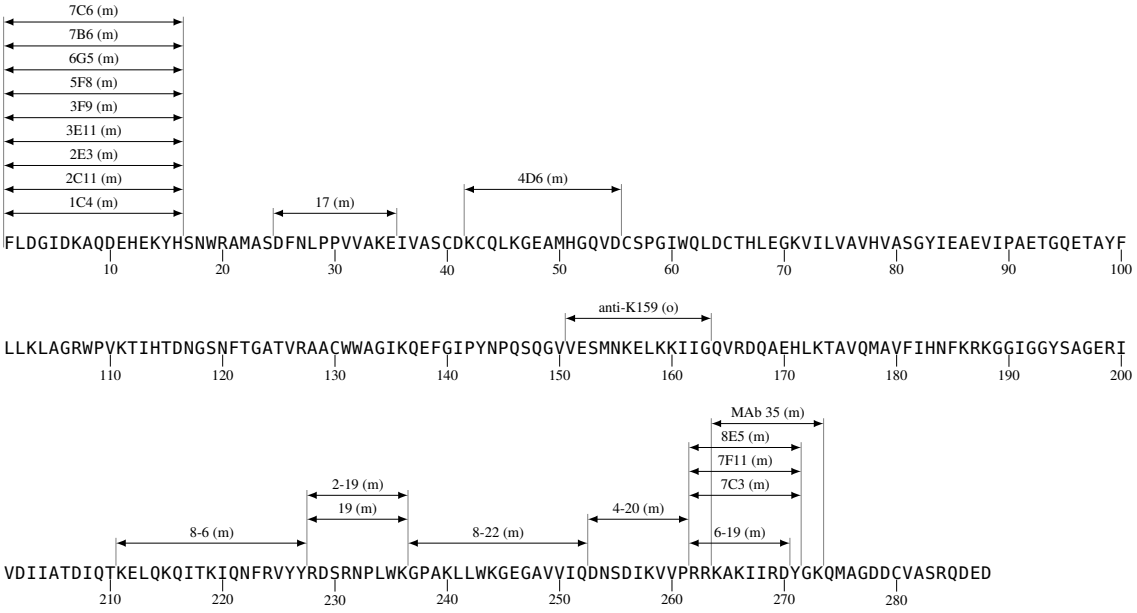


IV-D-6 RT Ab Epitope Map

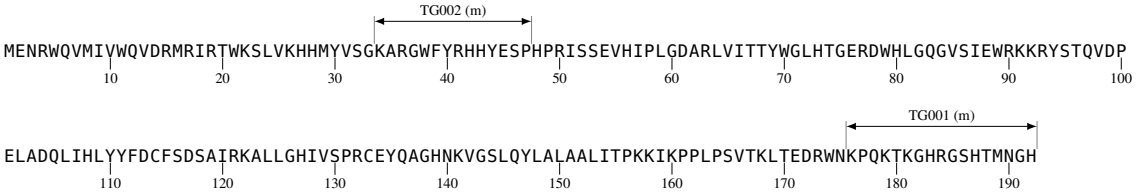




IV-D-7 Integrase Ab Epitope Map

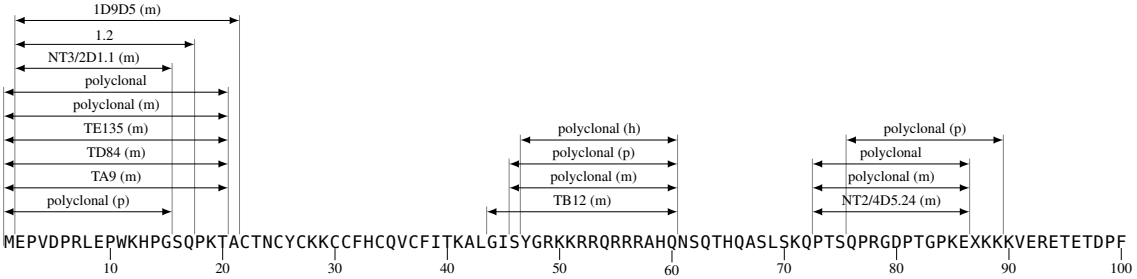


IV-D-8 Vif Ab Epitope Map

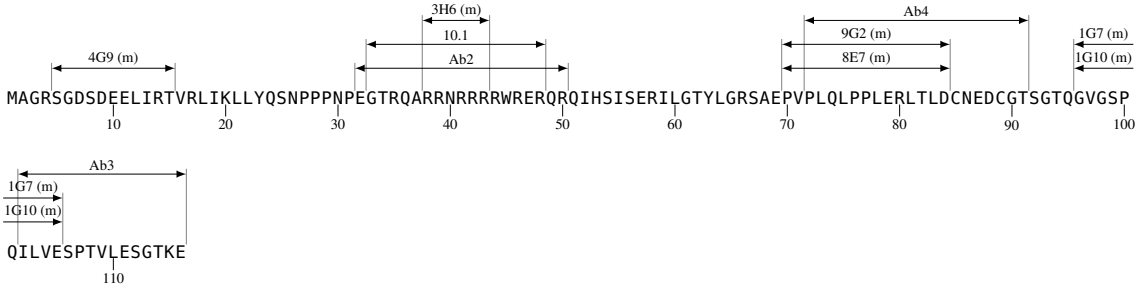


IV-D-9 Vpr Ab Epitope Map

IV-D-10 Tat Ab Epitope Map

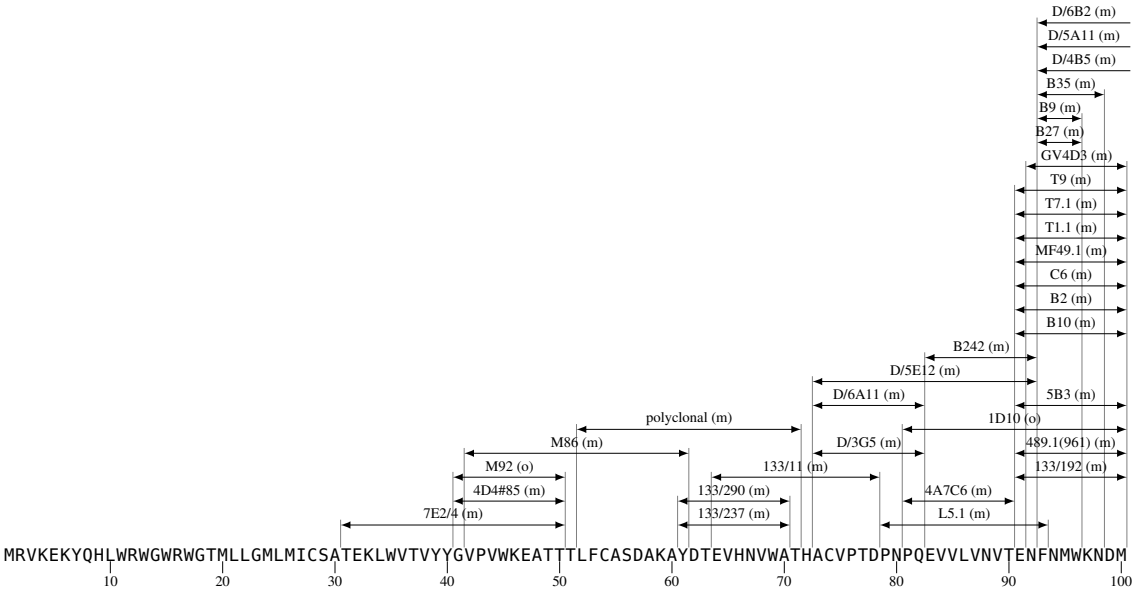


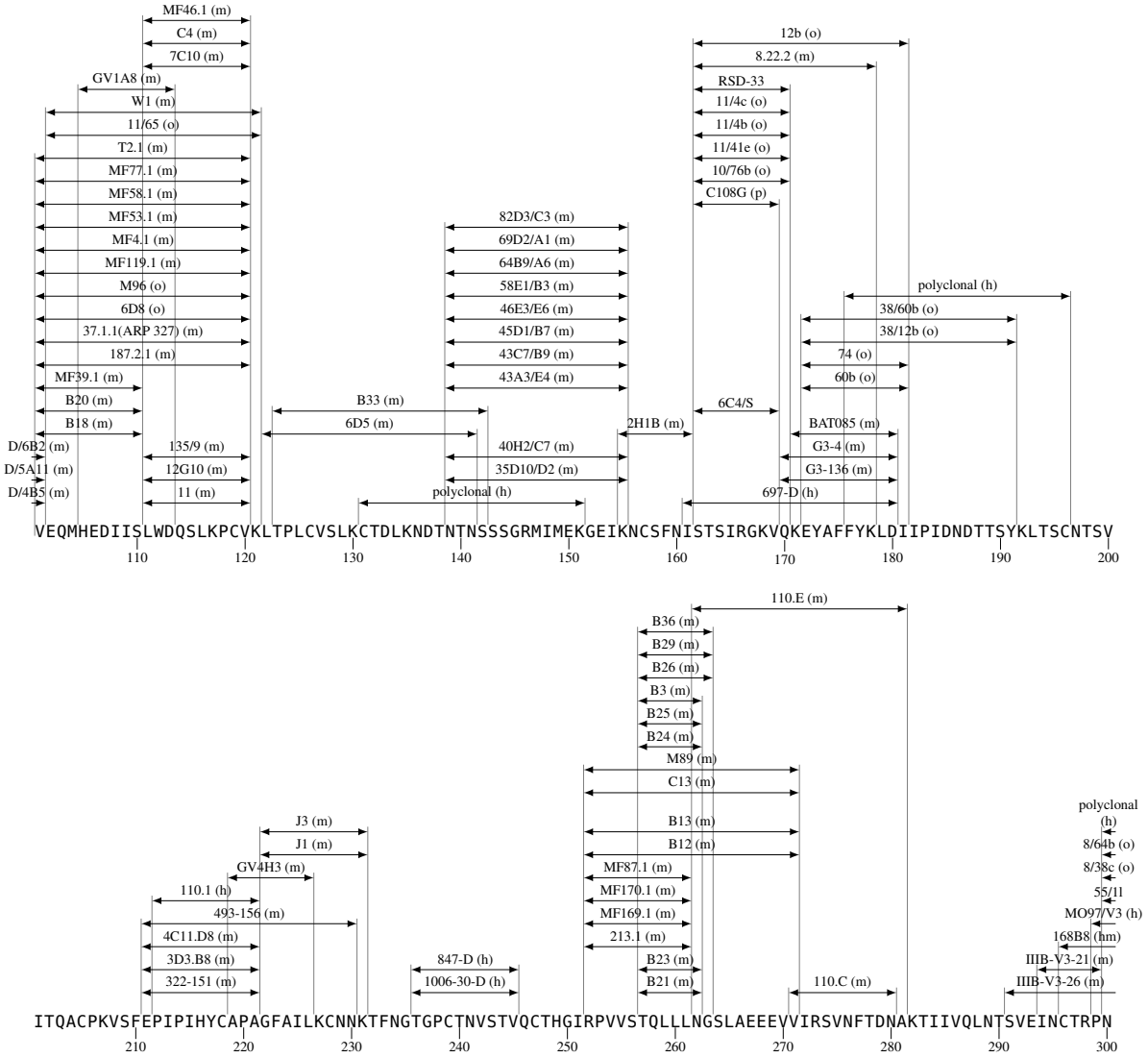
IV-D-11 Rev Ab Epitope Map



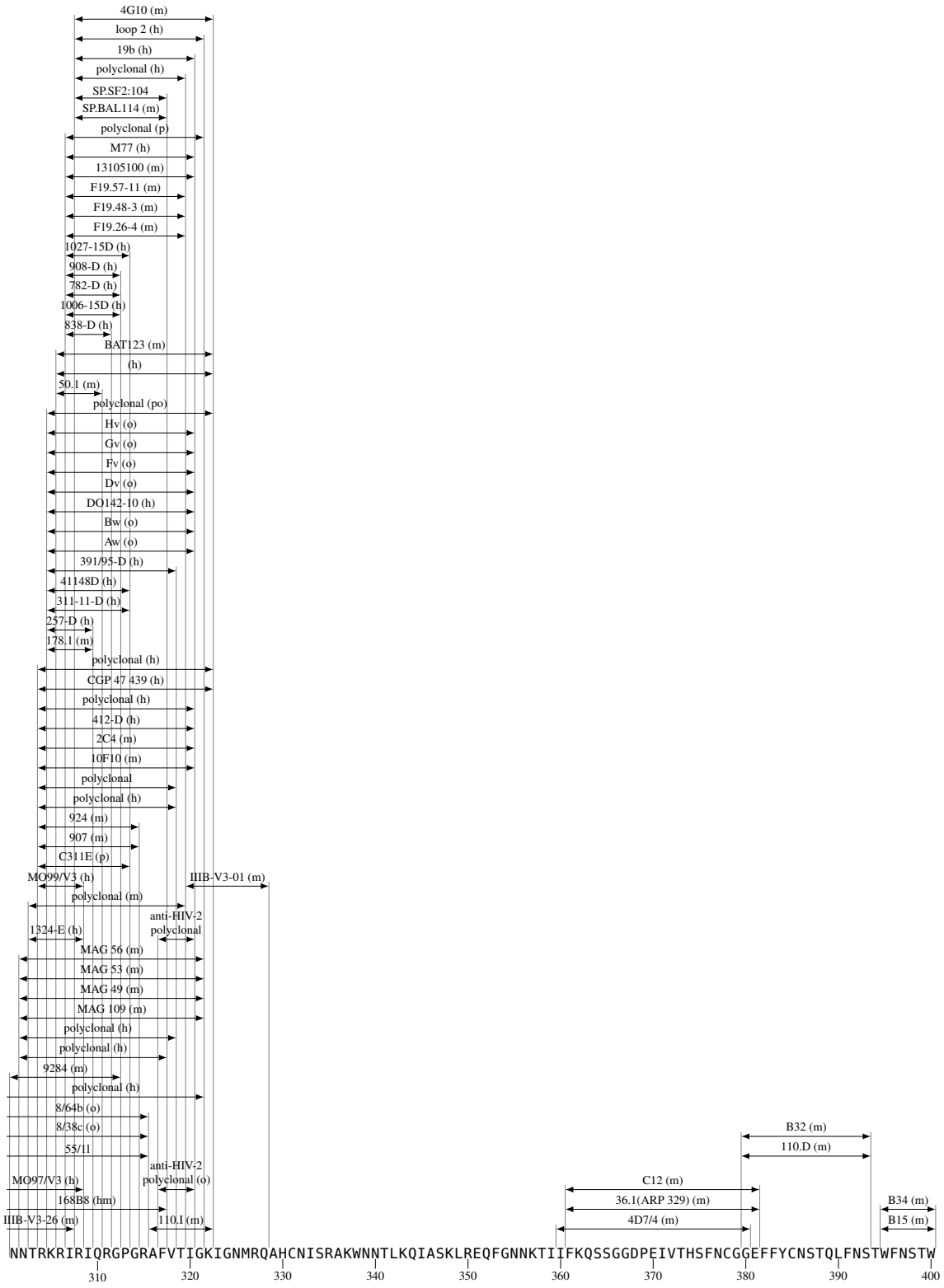
IV-D-12 Vpu Ab Epitope Map

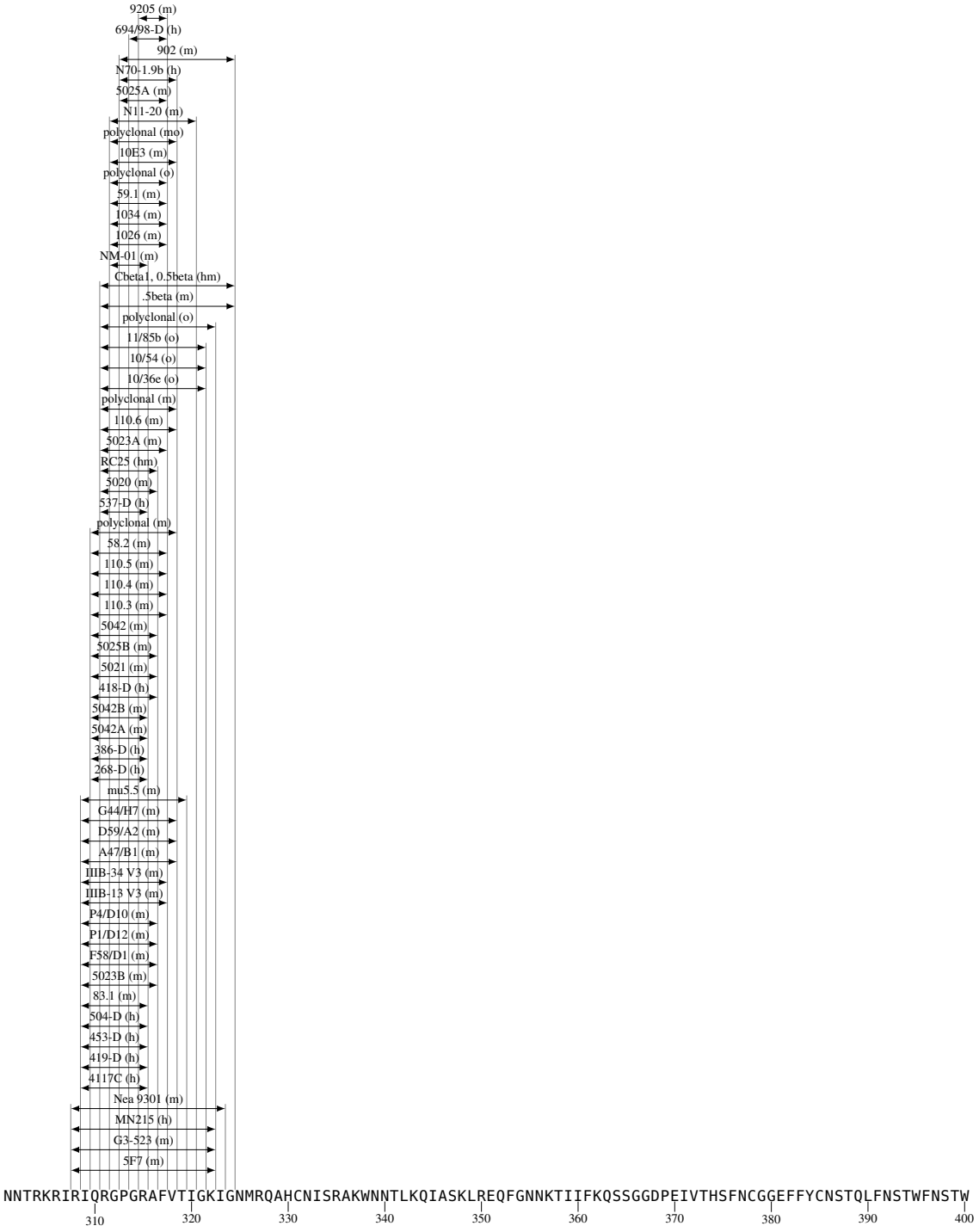
IV-D-13 gp160 Ab Epitope Map




MF46.1 (m)
C4 (m)
7C10 (m)
GV1A8 (m)
W1 (m)
11/65 (o)
T2.1 (m)
MF77.1 (m)
MF58.1 (m)
MF53.1 (m)
MF4.1 (m)
MF119.1 (m)
M96 (o)
6D8 (o)
37.1.1(ARP 327) (m)
187.2.1 (m)
MF39.1 (m)
B20 (m)
B18 (m)
D/6B2 (m)
D/5A11 (m)
D/4B5 (m)
135/9 (m)
12G10 (m)
11 (m)
B33 (m)
6D5 (m)
82D3/C3 (m)
69D2/A1 (m)
64B9/A6 (m)
58E1/B3 (m)
46E3/E6 (m)
45D1/B7 (m)
43C7/B9 (m)
43A3/E4 (m)
40H2/C7 (m)
35D10/D2 (m)
polyclonal (h)
12b (o)
8.22.2 (m)
RSD-33
11/4c (o)
11/4b (o)
11/41e (o)
10/76b (o)
C108G (p)
2H1B (m)
6C4/S
697-D (h)
polyclonal (h)
38/60b (o)
38/12b (o)
74 (o)
60b (o)
BAT085 (m)
G3-4 (m)
G3-136 (m)
VEQMHEDIISLWDQSLKPCVKLTPLCVSLKCTDLKNDTNTNSSSGRMIMEKGEIKNCSFNISTSIRGKVQKEYAFFYKLDIIPIDNDTTSYKLTSCNTSV
110
120
130
140
150
160
170
180
190
200
110.E (m)
B36 (m)
B29 (m)
B26 (m)
B3 (m)
B25 (m)
B24 (m)
M89 (m)
C13 (m)
B13 (m)
B12 (m)
MF87.1 (m)
MF170.1 (m)
MF169.1 (m)
213.1 (m)
B23 (m)
B21 (m)
110.C (m)
J3 (m)
J1 (m)
GV4H3 (m)
110.1 (h)
493-156 (m)
4C11.D8 (m)
3D3.B8 (m)
322-151 (m)
847-D (h)
1006-30-D (h)
polyclonal (h)
8/64b (o)
8/38c (o)
55/11
MO97/V3 (h)
168B8 (hm)
IIIB-V3-21 (m)
IIIB-V3-26 (m)
ITQACPKVSFEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVSTVQCTHGIRPVVSTQLLLNGSLAEEEVVIRSVNFTDNAKTIIVQLNTSVEINCTRPN
210
220
230
240
250
260
270
280
290
300

B Cell


4G10 (m)
loop 2 (h)
19b (h)
polyclonal (h)
SP.SF2:104
SP.BAL114 (m)
polyclonal (p)
M77 (h)
13105100 (m)
F19.57-11 (m)
F19.48-3 (m)
F19.26-4 (m)
1027-15D (h)
908-D (h)
782-D (h)
1006-15D (h)
838-D (h)
BAT123 (m)
(h)
50.1 (m)
polyclonal (po)
Hv (ϕ)
Gv (ϕ)
Fv (ϕ)
Dv (ϕ)
DO142-10 (h)
Bw (ϕ)
Aw (ϕ)
391/95-D (h)
41148D (h)
311-11-D (h)
257-D (h)
178.1 (m)
polyclonal (h)
CGP 47 439 (h)
polyclonal (h)
412-D (h)
2C4 (m)
10F10 (m)
polyclonal
polyclonal (h)
924 (m)
907 (m)
C311E (p)
MO99/V3 (h)
IIIB-V3-01 (m)
polyclonal (m)
anti-HIV-2 polyclonal
1324-E (h)
MAG 56 (m)
MAG 53 (m)
MAG 49 (m)
MAG 109 (m)
polyclonal (h)
polyclonal (h)
9284 (m)
polyclonal (h)
8/64b (ϕ)
8/38c (ϕ)
55/11
anti-HIV-2 polyclonal (ϕ)
MO97/V3 (h)
168B8 (hm)
IIIB-V3-26 (m)
110.I (m)
B32 (m)
110.D (m)
C12 (m)
36.1(ARP 329) (m)
4D7/4 (m)
B34 (m)
B15 (m)
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLREQFGNNKTIIFKQSSGGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTW
310
320
330
340
350
360
370
380
390
400


9205 (m)
694/98-D (h)
902 (m)
N70-1.9b (h)
5025A (m)
N11-20 (m)
polyclonal (mo)
10E3 (m)
polyclonal (o)
59.1 (m)
1034 (m)
1026 (m)
NM-01 (m)
Cbeta1, 0.5beta (hm)
.5beta (m)
polyclonal (o)
11/85b (o)
10/54 (o)
10/36e (o)
polyclonal (m)
110.6 (m)
5023A (m)
RC25 (hm)
5020 (m)
537-D (h)
polyclonal (m)
58.2 (m)
110.5 (m)
110.4 (m)
110.3 (m)
5042 (m)
5025B (m)
5021 (m)
418-D (h)
5042B (m)
5042A (m)
386-D (h)
268-D (h)
mu5.5 (m)
G44/H7 (m)
D59/A2 (m)
A47/B1 (m)
IIIB-34 V3 (m)
IIIB-13 V3 (m)
P4/D10 (m)
P1/D12 (m)
F58/D1 (m)
5023B (m)
83.1 (m)
504-D (h)
453-D (h)
419-D (h)
4117C (h)
Nea 9301 (m)
MN215 (h)
G3-523 (m)
5F7 (m)
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLREQFGNNKTIIFKQSSGGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTW
310
320
330
340
350
360
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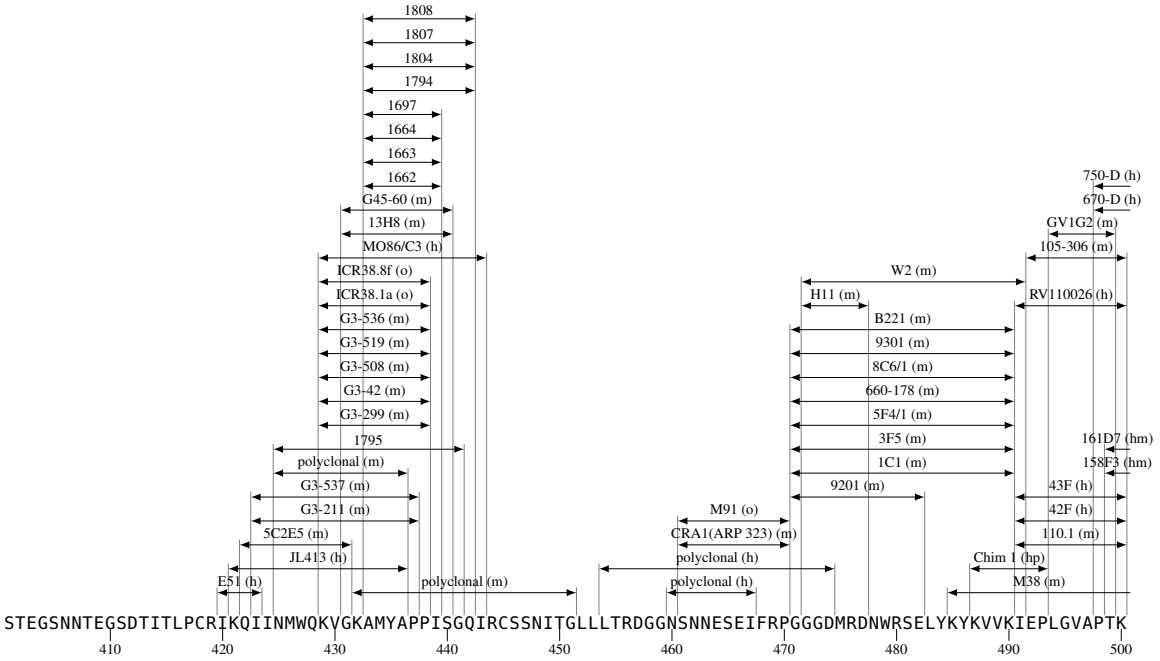
380
390
400

B Cell


1808
1807
1804
1794
1697
1664
1663
1662
G45-60 (m)
13H8 (m)
MO86/C3 (h)
ICR38.8f (o)
ICR38.1a (o)
G3-536 (m)
G3-519 (m)
G3-508 (m)
G3-42 (m)
G3-299 (m)
1795
polyclonal (m)
G3-537 (m)
G3-211 (m)
5C2E5 (m)
JL413 (h)
E51 (h)
polyclonal (m)
M91 (o)
CRA1(ARP 323) (m)
polyclonal (h)
polyclonal (h)
W2 (m)
H11 (m)
B221 (m)
9301 (m)
8C6/1 (m)
660-178 (m)
5F4/1 (m)
3F5 (m)
1C1 (m)
9201 (m)
750-D (h)
670-D (h)
GV1G2 (m)
105-306 (m)
RV110026 (h)
161D7 (hm)
158F3 (hm)
43F (h)
42F (h)
110.1 (m)
Chim 1 (hp)
M38 (m)
STEGSNNTEGSDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNITGLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTK
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430
440
450
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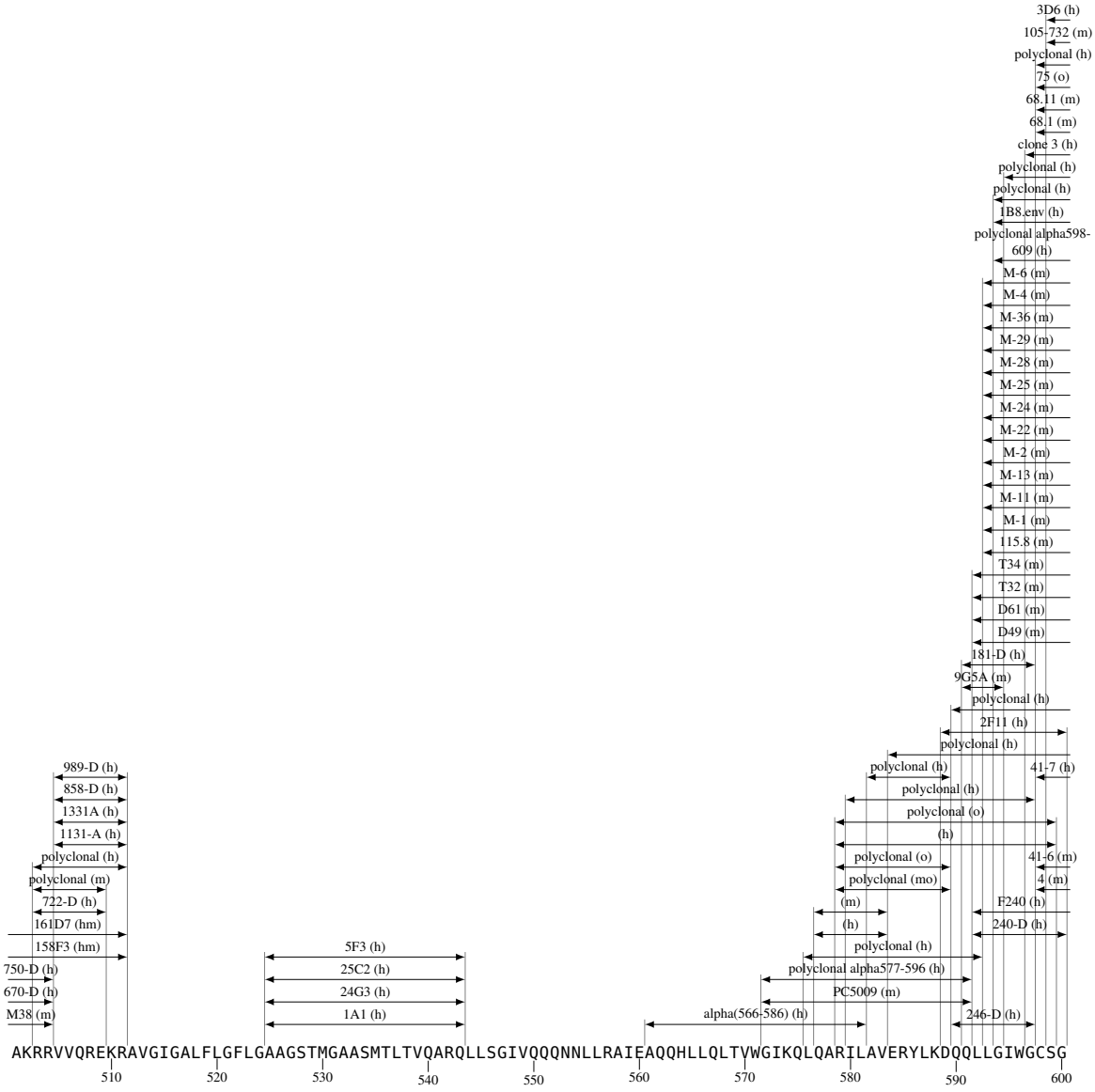
490
500

B Cell


3D6 (h)
105-732 (m)
polyclonal (h)
75 (o)
68.11 (m)
68.1 (m)
clone 3 (h)
polyclonal (h)
polyclonal (h)
1B8.env (h)
polyclonal alpha598-609 (h)
M-6 (m)
M-4 (m)
M-36 (m)
M-29 (m)
M-28 (m)
M-25 (m)
M-24 (m)
M-22 (m)
M-2 (m)
M-13 (m)
M-11 (m)
M-1 (m)
115.8 (m)
T34 (m)
T32 (m)
D61 (m)
D49 (m)
181-D (h)
9G5A (m)
polyclonal (h)
2F11 (h)
polyclonal (h)
989-D (h)
858-D (h)
1331A (h)
1131-A (h)
polyclonal (h)
polyclonal (m)
722-D (h)
161D7 (hm)
158F3 (hm)
750-D (h)
670-D (h)
M38 (m)
5F3 (h)
25C2 (h)
24G3 (h)
1A1 (h)
polyclonal (h)
41-7 (h)
polyclonal (h)
polyclonal (o)
(h)
polyclonal (o)
41-6 (m)
polyclonal (mo)
4 (m)
(m)
F240 (h)
(h)
240-D (h)
polyclonal (h)
polyclonal alpha577-596 (h)
PC5009 (m)
alpha(566-586) (h)
246-D (h)
AKRRVVQREKRAVGIGALFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
510
520
530
540
550
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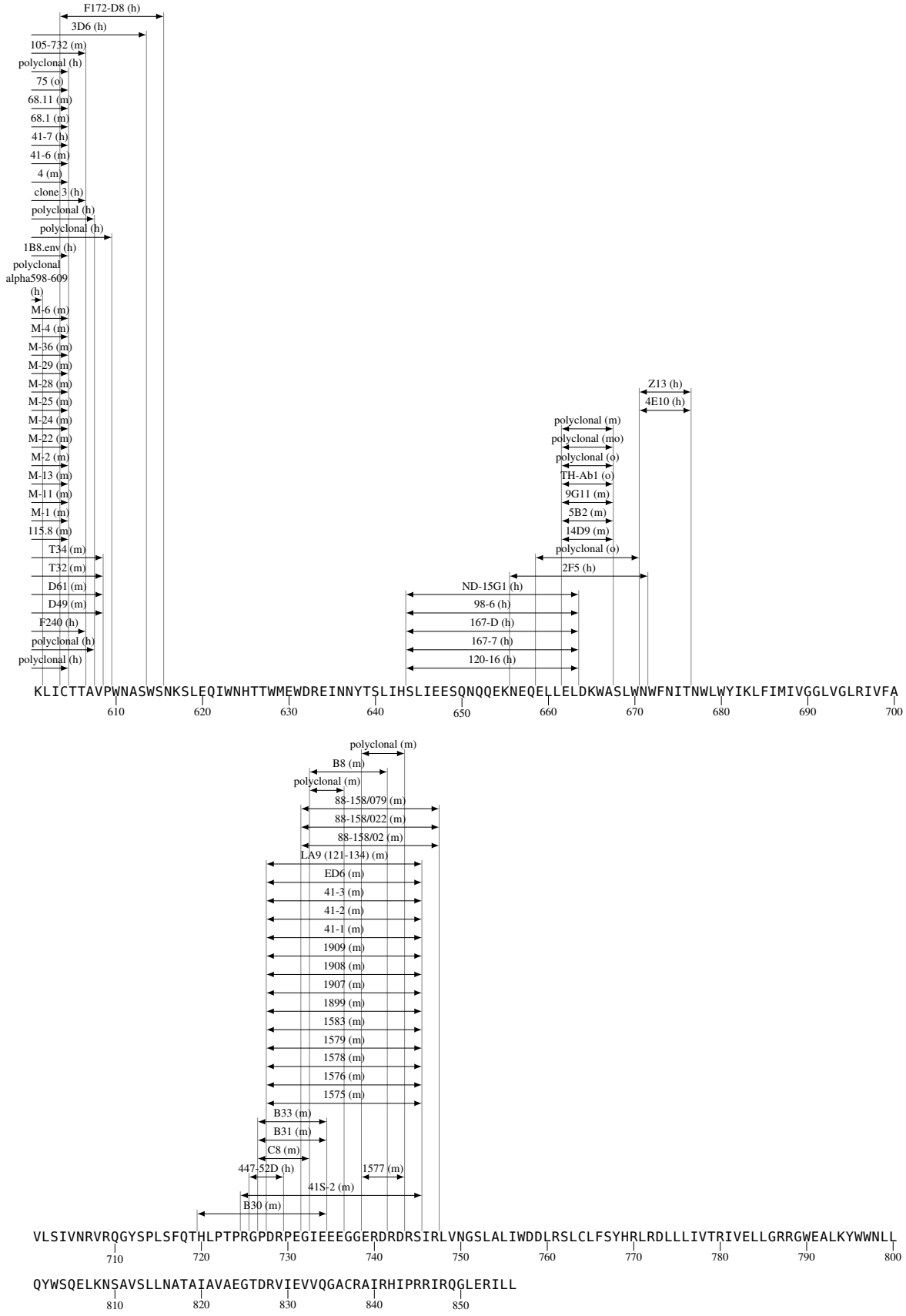
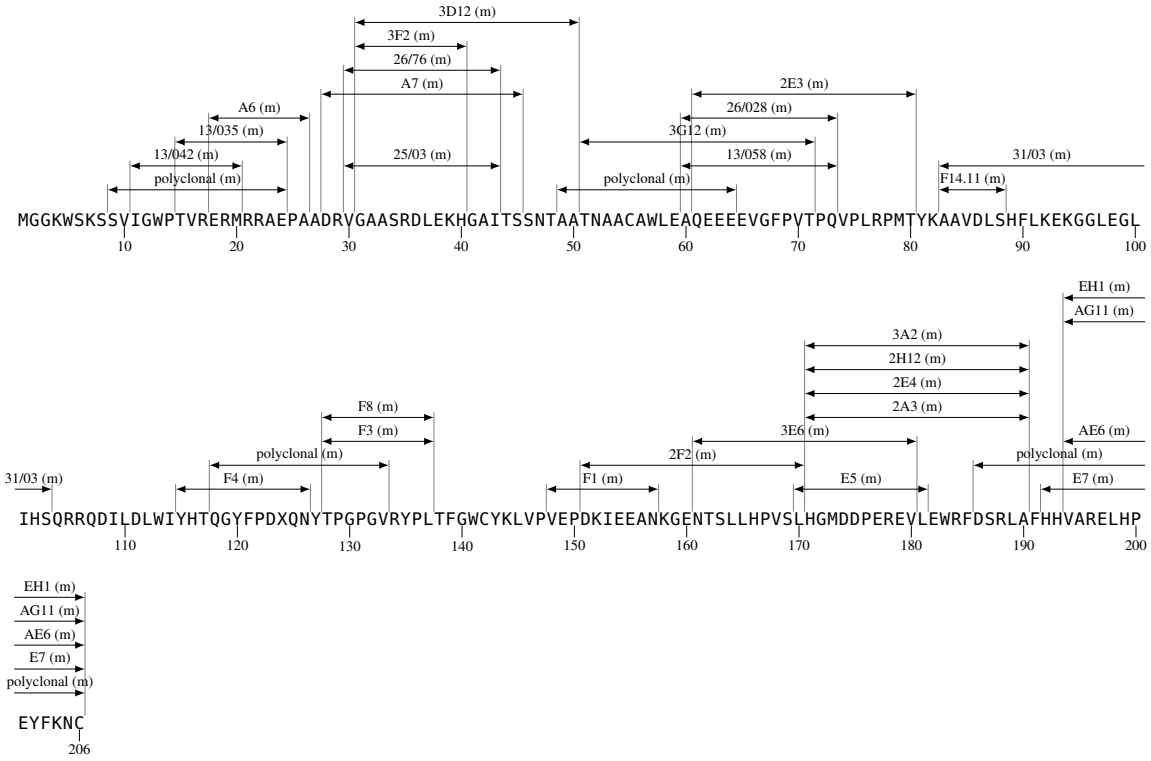
570
580
590
600


F172-D8 (h)
3D6 (h)
105-732 (m)
polyclonal (h)
75 (o)
68.11 (m)
68.1 (m)
41-7 (h)
41-6 (m)
4 (m)
clone 3 (h)
polyclonal (h)
polyclonal (h)
1B8.env (h)
polyclonal alpha598-609 (h)
M-6 (m)
M-4 (m)
M-36 (m)
M-29 (m)
M-28 (m)
M-25 (m)
M-24 (m)
M-22 (m)
M-2 (m)
M-13 (m)
M-11 (m)
M-1 (m)
115.8 (m)
T34 (m)
T32 (m)
D61 (m)
D49 (m)
F240 (h)
polyclonal (h)
polyclonal (h)
Z13 (h)
4E10 (h)
polyclonal (m)
polyclonal (mo)
polyclonal (o)
TH-Ab1 (o)
9G11 (m)
5B2 (m)
14D9 (m)
polyclonal (o)
2F5 (h)
ND-15G1 (h)
98-6 (h)
167-D (h)
167-7 (h)
120-16 (h)
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWFNITNWLWYIKLFIMIVGGLVGLRIVFA
610 620 630 640 650 660 670 680 690 700
polyclonal (m)
B8 (m)
polyclonal (m)
88-158/079 (m)
88-158/022 (m)
88-158/02 (m)
LA9 (121-134) (m)
ED6 (m)
41-3 (m)
41-2 (m)
41-1 (m)
1909 (m)
1908 (m)
1907 (m)
1899 (m)
1583 (m)
1579 (m)
1578 (m)
1576 (m)
1575 (m)
B33 (m)
B31 (m)
C8 (m)
447-52D (h)
1577 (m)
41S-2 (m)
B30 (m)
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVNGSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
710 720 730 740 750 760 770 780 790 800
QYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQGACRAIRHIPRRIRQGLERILL
810 820 830 840 850

B Cell

IV-D-14 Nef Ab Epitope Map



Part V

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